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FINAL SUBMISSION OF
THE CANADIAN RED CROSS SOCIETY

TO THE

COMMISSION OF INQUIRY ON THE

BLOOD SYSTEM IN CANADA

December 6, 1996

Volume 3 of 4



The Canadian Red Cross Society

**COMMISSION OF INQUIRY ON THE
BLOOD SYSTEM IN CANADA**

**THE CANADIAN RED CROSS SOCIETY
SUBMISSIONS**

VOLUME III

**PART III
Sections F - H
and PART IV**

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December 6, 1996

Government
Publication

COMMISSION ON POLICE IN THE
GOOD POLICE IN CANADA

THE CANADIAN RED CROSS SOCIETY

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COMMISSION OF INQUIRY ON THE
BLOOD SYSTEM IN CANADA

THE CANADIAN RED CROSS SOCIETY
SUBMISSIONS

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F. HEAT-TREATMENT

1) Introduction

747. The CRCS endeavoured to obtain the best quality and safest factor concentrate for Canadian hemophiliacs. It carefully monitored the early development of heat-treated concentrate and lent support to its implementation when, in the fall of 1984, sufficient data became available establishing its effectiveness in disabling the putative AIDS virus, HTLV-III. To ensure its implementation the CRCS was instrumental in co-ordinating the December 10, 1984 Consensus Conference that recommended various measures to ensure a smooth transition to heat-treated concentrate. In accordance with these recommendations, the CRCS acted promptly and overcame substantial regulatory and supply problems in order to make heat-treated Factor VIII and Factor IX available.

748. When technical advances improved the heat-treatment process, the CRCS once again moved expeditiously to overcome regulatory and supply hurdles. Through its efforts, the CRCS successfully averted the effect of world wide shortages and secured a sufficient Canadian supply. As a result, Canadian hemophiliacs were among the first in the world to have universal access to this state- of-the-art concentrate.

749. Details of the CRCS efforts to acquire and implement heat-treated Factor VIII and Factor IX including measures taken to overcome various obstacles that impeded the implementation are set out below.

2) Development of the Heat-Treatment Process

a) **Early Attempts**

750. The heating of blood plasma factors is not a new technology. Albumin has been routinely heated to inactivate hepatitis and other viruses since the 1950's using a process similar to the pasteurization of milk. However, a heat-treatment process for clotting factor, being much more complex, was not developed until the early 1980's. The process was difficult to develop because the Factor VIII protein molecule is heat sensitive and any heat-treatment process affects the potency of the finished concentrate. While the protein could be stabilized, any process which stabilized the protein also stabilized any viruses or bacteria present. As technology developed, the challenge was to find a method whereby viruses were inactivated but the Factor VIII activity was left relatively intact.¹⁴³⁷

751. The early attempts to heat-treat concentrate were designed to reduce the risk of hepatitis, not AIDS.¹⁴³⁸ When the first cases of AIDS in hemophiliacs were reported, research into methods of viral inactivation of Factor VIII concentrate was still in a developmental stage. The technological limits of the process were acknowledged by the NHF MSAC at its January 14, 1983 meeting. This body recommended that fractionators "expedite the development of processing methods that will inactivate viruses potentially present in Factor VIII concentrate." Dr. Derrick, who attended this meeting, reported that the discussion of inactivation of a possible AIDS agent in concentrate did not result in any practical outcome. Although it was hoped that heat-treating might be utilized to prevent the possible transmission of a yet undiscovered AIDS agent, the inactivation of hepatitis was still the focus of industry research.¹⁴³⁹

¹⁴³⁷ *Evidence of Dr. Davey, former Assistant National Director BTS, pp. 26520-26522.*

¹⁴³⁸ *Ex. 935, Vol. 234, Tab 11 (May 24, 1983, Cutter Memo from M.M. Sternberg to Dr. Schaeffler, Dr. Fischer, Jan Hjorth re: Pasteurization of Plasma Products).*

¹⁴³⁹ *Ex. 616, Vol. 13, Tab 11 (January 14, 1983 National Hemophilia Foundation - Recommendations to Prevent AIDS in Patients with Hemophilia); and*

b) **Inhibitors**

752. The CRCS and hemophilia treaters were concerned that the heat-treatment process would destroy the concentrate's effectiveness and pose a serious health risk for many hemophiliacs. This concern stemmed from the fact that the heating process could alter the Factor VIII protein molecule and might cause the body to create "inhibitors" or antibodies to the altered molecule.¹⁴⁴⁰ If this occurred not only would the antibodies destroy the infused Factor VIII, but they also destroyed any Factor VIII that was produced naturally in the body.¹⁴⁴¹ As one hemophiliac testified, this resulted in "an absolute zero in coagulation".¹⁴⁴²

753. Hemophiliacs who developed inhibitors had to infuse enormous quantities of Factor VIII concentrate in the hopes of raising clotting levels to a point where the inhibitor was "overwhelmed". While the average severe hemophiliac without inhibitors would infuse approximately 50,000 - 60,000 units per year,¹⁴⁴³ it would not be unusual for a hemophiliac with inhibitors to infuse with the same quantity in a single day.¹⁴⁴⁴

Ex. 616, Vol. 13, Tab 12 (January 14, 1983, Trip Report by Dr. Derrick).

¹⁴⁴⁰ *Evidence of Dr. Zuck, former Director of Division of Blood and Blood Products, FDA, p. 22892.*

¹⁴⁴¹ *Evidence of Bob Verreau, Hemophiliac, p. 6991; and*

Evidence of Don Huneault, Hemophiliac, pp. 3872-3874.

¹⁴⁴² *Evidence of Dan Huneault, Hemophiliac, pp. 3872-3874.*

¹⁴⁴³ *Ex. 811, Vol. 182, Part 1, Tab 3, pp. 33 - 34 (April 17, 1980, CHS Report); see also Ex. 750, Vol. 157, Tab 67 (October 1, 1981, Letter from Dr. Grave to Dr. Derrick).*

¹⁴⁴⁴ *Evidence of Dr. Inwood, Hemophilia Treater, pp. 33687-33691; and*

Evidence of Dr. Davey, former Assistant National Director BTS, pp. 26443 - 26444.

754. Several treaters testified that they were very concerned about the serious health risk posed by inhibitors which, as Dr. Inwood testified, developed in 10 - 15% of hemophiliacs.¹⁴⁴⁵ Dr. Strawczynski testified that in 1982 inhibitors were still the number one problem in hemophilia and constituted the most severe complication of treatment.¹⁴⁴⁶ Dr. Card and Dr. Rivard testified that the development of inhibitors was one of the most serious issues with which a treater had to be concerned.¹⁴⁴⁷ Dr. Boucher of the BoB confirmed that treaters and patients were almost as concerned about inhibitors as they were about viral infections.¹⁴⁴⁸

c) Loss of Yield

755. One of the key problems associated with this developing technology was the substantial loss of yield of the finished concentrate. Prior to 1984, early attempts to heat-treat concentrate could result in a loss of 25 - 30% in yield; even the most advanced heat-treatment process reduced yield by 10%.¹⁴⁴⁹ Reduced yield had significant self-sufficiency and cost implications. Adopting the heat-treatment process for Canadian-source products would have necessitated collecting substantially more volunteer plasma in order to maintain the same level of self-sufficiency. Not only was there a cost to collecting the additional plasma required, but the heat-treatment process was more expensive than regular fractionation. Lowered yields, in combination with blood shortages and a shrinking donor base, would necessitate purchasing even more foreign, potentially riskier, commercial plasma. Prior to 1984, without sufficient

¹⁴⁴⁵ Evidence of Dr. Inwood, *Hemophilia Treater*, p. 33688.

¹⁴⁴⁶ Evidence of Dr. Strawczynski, *former MSAC Chairman and Hemophilia Treater, Montreal Hospital*, p. 31300.

¹⁴⁴⁷ Evidence of Dr. Card, *former Member of the CHS MSAC*, p. 31891; and

Evidence of Dr. Rivard, *Director Hematology Laboratories, Hospital Ste.-Justine, Montreal*, pp. 35028 - 35031.

¹⁴⁴⁸ Evidence of Dr. Boucher, *BoB Panel*, pp. 43672 - 43673.

¹⁴⁴⁹ Evidence of Dr. Perrault, *former National Director BTS*, pp. 26697-26698.

assurance of effective virus inactivation, the CRCS and the BoB were naturally reluctant to endorse an experimental process that incurred a potential inhibitor problem, reduced yields and additional costs which could compromise long range plans for Canadian self-sufficiency.¹⁴⁵⁰

d) **Assessing Evidence of Viral Inactivation**

756. Like the CBC, BoB, CHS MSAC and many hemophilia treaters, the CRCS was not prepared to recommend the heat-treatment process until there was sufficient evidence demonstrating that it was effective in inactivating infectious viruses. As the distributor of blood products for Canadian hemophiliacs, CRCS closely followed the development of the heat-treatment process.

757. Hyland was the first fractionator to market a heat-treatment process. Hyland claimed that its process, which was licensed in the United States in 1983, significantly reduced the risk of transmitting hepatitis B and NANB. However, Hyland failed to provide any evidence showing that their "Hemophil-T" concentrate actually eliminated the risk of hepatitis transmission. At best, Hyland could claim that its process reduced the risk of transmission. While Hyland based its claim on a study it conducted on chimpanzees,¹⁴⁵¹ the study was regarded as inconclusive and seriously flawed. In a group of chimpanzees who received AHF tainted with large doses of hepatitis B virus, subjects who were given Hyland's heat-treated concentrate *developed* hepatitis, while subjects who received the non-heat-treated AHF did not.

758. In that same study, a second group of chimpanzees received AHF seeded with much smaller doses of hepatitis B than subjects receiving Hyland's heat-treated AHF, and did

¹⁴⁵⁰ Ex. 620, Volume 17, Tab 13, p. 3 (July 25, 1983 Minutes of A Meeting Held Between Members of the BoB and the CRCS BTS).

¹⁴⁵¹ Ex. 622, Vol. 19, Tab 5, pp. 026288-026289 (Travenol Canada, Fenwal Division Proposal November 23, 1983 RFP 006-83).

not appear to develop hepatitis within the same four-month time period as chimpanzees who received the untreated product. However, even these animals subsequently developed hepatitis B markers after 7½ - 10 months.¹⁴⁵² Hyland conceded that Hemophil-T was capable of transmitting hepatitis.¹⁴⁵³

759. Cutter was doubtful about its competitor's claims and recognized the need to pursue a process that was truly effective in inactivating viruses. A May 24, 1983 internal Cutter memo noted that Hyland's U.S. license was granted hastily without proper supporting evidence:

On a short term we are facing a crisis. Our competitors have succeeded to come out first with a limited claim product. Forced by circumstances, the FDA *granted approval without asking for solid evidence*, as they asked Cutter two years ago. It is clear, that we have to fight the fire with a short term solution that will preserve our market position but not relent work and resources to be able to claim freedom from contamination by disease causing agents.¹⁴⁵⁴
[Emphasis added]

760. The CHS MSAC and Canadian hemophilia treaters also expressed reservations about Hyland's heat-treated concentrate. On August 10, 1983, Dr. Strawczynski, Chair of the CHS MSAC met with Dr. Naylor to discuss the drawbacks of Hyland's process. The CRCS indicated its willingness to follow the advice of the MSAC as to whether or not Hemophil-T should be purchased.¹⁴⁵⁵ Dr. Strawczynski undertook to solicit further information and in September 1983 she wrote to all MSAC members requesting their opinions on the issue. In so

¹⁴⁵² Ex. 622, Vol. 19, Tab 5 (*Travenol Canada Inc. Fenwal Division Proposal R.F.P. 006-83 Hemophil T Anti-hemophilic Factor (Human) Method Four - Heat Treated*) November 23, 1983; and

Ex. 938, Vol. 233, Tab 30, p. 26305 (*Travenol Canada Inc. Fenwal Division Hemofil T Anti hemophilic Factor (Human) Method Four - Heat Treated*).

¹⁴⁵³ Ex. 938, Vol. 233, Tab 42, p.00144 (*Travenol Canada, Fenwal Division, Proposal RFP 006-84, Product Monograph*).

¹⁴⁵⁴ Ex. 935, Vol. 234, Tab 11 (*May 24, 1983 Cutter Memo from M.M. Sternberg to Dr. Schaeffler, Dr. Fischer, Jan Hjorth re: Pasteurization of Plasma Products*).

¹⁴⁵⁵ Ex. 754, Vol. 160, Tab 63 (*August 15, 1983, Memo from Dr. Naylor to File re: Telephone Conversation with Dr. Strawczynski on August 10, 1983*).

doing, Dr. Strawczynski noted "there is not convincing evidence yet that this product is hepatitis free". She also expressed the concerns of the CRCS about reduced yields and higher costs.¹⁴⁵⁶

761. On September 8, 1983 Dr. Kaiser Ali, a hemophiliac treater from the Newfoundland Hemophilia Comprehensive Care Centre, wrote to Dr. Strawczynski. Dr. Ali saw no advantage in switching to a higher priced product "simply to satisfy the financial aspirations of the manufacturer". In his opinion, the regular non-heat-treated Factor VIII concentrate was the treatment of choice.¹⁴⁵⁷

762. On September 21, 1983 a group of pediatric haematologists and oncologists met and discussed the proposed use of Hyland's Hemophil-T. At the meeting, several important hemophilia treaters were present including Dr. Card, Dr. Inwood, Dr. Poon and Dr. Ali. In their opinion, Hemophil-T was not superior to other non-heat-treated commercial concentrates available at that time. The hemophilia treaters did not endorse Hemophil-T because the data suggested that it was not totally effective in inactivating the hepatitis virus. In addition, concerns were expressed about the potential development of inhibitors, and the substantial loss of factor activity as a result of the heat-treatment process.¹⁴⁵⁸

763. In response to an October 1983 CRCS request for proposal, Hyland submitted its Hemophil-T concentrate for consideration. Hemophil-T compared poorly with the concentrate of other fractionators. In addition to the lack of evidence of hepatitis inactivation, Hemophil-T fell short of other products in the following areas:¹⁴⁵⁹

¹⁴⁵⁶ Ex. 755, Vol. 161, Tab 1 (September 1983, Memo from Dr. Strawczynski, Chairperson to All MSAC Members).

¹⁴⁵⁷ Ex. 755, Vol. 161, Tab 13 (September 9, 1983 Letter from Dr. S.K. Ali to Dr. Strawczynski).

¹⁴⁵⁸ Evidence of Dr. Poon, Deputy Medical Director, Calgary Centre, pp. 34452 - 34454; and

Evidence of Dr. Kaiser Ali, Pediatrician, Hemophilia Treater, p. 32631.

¹⁴⁵⁹ Ex. 622, Vol. 19, Tab 14, pp. 50255, 50258, 50261 (1984 AHF Concentrate Comparison Documents).

- reconstitution time;
- percentage of fibrinogen;
- specific activity of international units of AHF per milligram of protein;
- price.

In light of the inconclusive evidence and Hyland's unsatisfactory performance relative to other proposals, the CRCS was not prepared to purchase Hemophil-T. At no time did Hyland claim that its concentrate was effective in inactivating the putative agent for AIDS.¹⁴⁶⁰

764. A promising development with respect to the heat-treatment process was the Cutter "Koate H.T.", which was licensed by the FDA for U.S. distribution on February 29, 1984.¹⁴⁶¹ Throughout the first half of 1984, the CRCS corresponded with Cutter about the development of this process.¹⁴⁶² On May 30, 1984, the CRCS met with representatives from Cutter to discuss its new process. Cutter was unable to assure the CRCS that there was an appreciable reduction in the risk of hepatitis transmission. Like Hemophil-T, the Cutter concentrate's yield was reduced 10 - 20%.¹⁴⁶³ There were reports about solubility problems

¹⁴⁶⁰ Evidence of Dr. Davey, former Assistant National Director BTS, pp. 26608 - 26614; and

Evidence of Micheline Pinard, Sales Rep. Hyland/Baxter/Fenwal, pp. 38936 - 38937.

¹⁴⁶¹ Ex. 932, Vol. 229, Tab 31 (February 29, 1984, Cutter, Division of Miles Laboratories, Ltd., New Release re: U.S. F.D.A. License to Sell Heat-Treated Anti-hemophilic Factor VIII Concentrate).

¹⁴⁶² Ex. 624, Vol. 21, Tab 7 (January 19, 1984, Letter from Mr. Ashworth, V.P. Scientific Affairs Cutter to Dr. Naylor);

Ex. 624, Vol. 21, Tab 25 (February 20, 1984, Memo from Mr. Anhorn to Dr. Naylor);

Ex. 626, Vol. 23, Tab 43 (June 6, 1984, Letter from Elias Green, Cutter to Dr. Naylor);

Ex. 627, Vol. 24, Tab 5 (June 14, 1984, Letter from Dr. Naylor to Elias Green, Cutter); and

Ex. 627, Vol. 24, Tab 14 (June 22, 1984, Letter from Dr. Naylor to Phil LeBlanc, Cutter).

¹⁴⁶³ Ex. 932, Vol. 229, Tab 40, pp. 50659-50660 (May 30, 1984, CRCS Blood Transfusion Service Minutes of Meeting of the BTS/Cutter Working Group); and

and in addition there was no evidence that inhibitors would not be formed as a result of the process.¹⁴⁶⁴ Nevertheless, the CRCS requested that Cutter forward any clinical data on its heat-treated concentrate for further evaluation and consideration.¹⁴⁶⁵

765. Hemophilia treaters had similar concerns about the potential risks of heat-treated concentrates. Among these concerns were loss in potency, and possible production of inhibitors.¹⁴⁶⁶ On May 5, 1984 the CHS MSAC met and discussed the merits of heat-treated concentrate. Handwritten notes attributing statements to Dr. Rivard recorded that heat-treated Factor VIII was still unproven, less effective, costly, still transmitted some hepatitis and had the additional drawback of reduced yield.¹⁴⁶⁷ The testimony of Dr. Poon confirmed that as a result of these and other concerns, the CHS MSAC did not recommend heat-treated factor concentrate at that time.¹⁴⁶⁸

766. On May 30, 1984 the CRCS agreed to adopt Cutter's new glycine precipitation step as soon as this process was licensed. Glycine precipitation was the foundation necessary to heat treat product as it enabled the removal of fibrogen. Cutter had written Dr. Naylor on January 19, 1984 to inform the CRCS that its custom-fractionated product could be produced with the glycine precipitated method.¹⁴⁶⁹ While Cutter did not know the effect this method

Ex. 932, Vol. 229, Tab 41, p. 50679 (May 30, 1984, Cutter Minutes of Meeting Held Between the CRCS and Cutter Laboratories).

¹⁴⁶⁴ *Ex. 932, Vol. 229, Tab 40, p. 50660 (May 30, 1984, CRCS Blood Transfusion Service Minutes of Meeting of the BTS/Cutter Working Group).*

¹⁴⁶⁵ *Ex. 932, Vol. 229, Tab 41, p. 50679 (May 30, 1984, Cutter Minutes of Meeting Held Between the CRCS and Cutter Laboratories).*

¹⁴⁶⁶ *Evidence of Dr. Elizabeth Ross, Medical Director, Charlottetown Centre, pp. 32646 - 32647.*

¹⁴⁶⁷ *Ex. 757, Vol. 163, Tab 10, p. 0675 (May 5, 1984, Minutes of Annual Meeting of MSAC of CHS).*

¹⁴⁶⁸ *Evidence of Dr. Poon, Deputy Medical Director, Calgary Centre, pp. 34452 - 34453.*

¹⁴⁶⁹ *Evidence of Jack Ryan, former President of Cutter Biologics, p. 38718.*

would have on yield,¹⁴⁷⁰ it was estimated to result in a 10% yield reduction.¹⁴⁷¹ In addition, at this time, the Cutter's heat-treated process had not yet been approved by the OoB. Cutter wanted all of its customers to consent to the glycine precipitate method because it would be easier to have all Factor VIII produced in its plant utilizing one process. Because of the uncertainty regarding the effect of this process on yield and the concerns in the early part of 1984 regarding the heat-treatment process, the CRCS advised Cutter that it should be discussed at a working group meeting between Cutter and the CRCS.¹⁴⁷²

767. At this working group meeting on May 30, 1984 it was determined that notwithstanding any decision on heat-treatment, the glycine precipitation step should be introduced for the production of Factor VIII.¹⁴⁷³ Formal confirmation of the consent of the CRCS to add the glycine precipitation step was sent to Cutter on June 22, 1984.¹⁴⁷⁴ By consenting to this new step in the Cutter manufacturing process, the CRCS determined that it would be in a better position to switch to heat-treated AHF in the event sufficient proof emerged demonstrating its effectiveness.¹⁴⁷⁵

768. In August 1984, Dr. Naylor attended the Sixteenth International Congress of World Federation of Hemophilia ("WHF") in Rio DeJaniero where methods of inactivating viruses were discussed. He reported that "These were rather disappointing sessions with relatively little in the way of new information". Most of the treatment methods reviewed caused Factor VIII recovery losses in the range of 10% - 20%. He noted that none of the studies

¹⁴⁷⁰ Ex. 932, Vol. 229, Tab 29 (January 19, 1984 letter from Dr. Ashwood to Dr. Naylor).

¹⁴⁷¹ Evidence of Dr. Davey, former Assistant National Director BTS, p. 26597.

¹⁴⁷² Ex. 932, Vol. 229, Tab 30 (February 20, 1984 Memo from Mr. Anhorn to Dr. Naylor).

¹⁴⁷³ Ex. 932, Vol. 229, Tab 40 (May 30, 1984 Minutes of a Meeting of the BTS/Cutter Working Group).

¹⁴⁷⁴ Ex. 932, Vol. 229, Tab 45 (June 22, 1984 Letter from Dr. Naylor to Mr. Leblanc).

¹⁴⁷⁵ Ex. 626, Vol. 23, Tab 41 (May 30, 1984 Minutes of Meeting of the BTS/Cutter Working Group); and

Ex. 627, Vol. 24, Tab 14 (June 22, 1984, Letter from Dr. Naylor to Mr. LeBlanc, Cutter).

presented demonstrated any proof whatsoever of HTLV-III inactivation. It was clear that much work had to be done in the area of treating blood products to effectively inactivate viruses.¹⁴⁷⁶ The foremost international hemophiliac treaters were at this conference and were members of the WHF Medical Board. In attendance were Dr. Shelby Dietrich, the Chair of the WHF MSAC, Dr. Allain, Dr. Martin Inwood from Canada, Dr. Levigne of the NHF MSAC, Professor Remde, Professor Schimph, and Dr. Youssef. The WHF Board discussed the merits of heat-treatment. Dr. Allain commented on the pressure which was being exerted by commercial companies to use heat-treated concentrates. The comments of Chairman, Shelby Dietrich were reported:

...considered that there was not sufficient information available to recommend the selection of any specific plasma product. She pointed out that heat treated concentrates were being used on previously untreated children in California and that additional data would be forthcoming... She urged caution, stressing the necessity for proper data, given the importance of this issue for the hemophilia community.¹⁴⁷⁷

769. The Board unanimously agreed on the following resolution concerning heat-treatment. The resolution read as follows:

THE MEDICAL BOARD REAFFIRMS ITS RECOMMENDATION PRESENTED AT THE STOCKHOLM GENERAL ASSEMBLY IN 1983 THAT: THERE IS INSUFFICIENT EVIDENCE TO RECOMMEND, AT THIS TIME, ANY CHANGE IN TREATMENT: THEREFORE, PRESENT TREATMENT OF HEMOPHILIA SHOULD CONTINUE WITH WHATEVER BLOOD PRODUCTS ARE AVAILABLE, ACCORDING TO THE JUDGMENT OF THE INDIVIDUAL PHYSICIAN

and further adds

THAT THERE IS A CRITICAL NEED FOR DATA ON THE OUTCOMES OF VARIOUS VIRAL ATTENUATION STRATEGIES OR PLASMA DERIVATIVES, AS TO BOTH THE DEVELOPMENT OF AIDS AND NON-

¹⁴⁷⁶ Ex. 758, Vol. 164, Tab 7, p. 038062 (August 24 - 28, 1984, Trip Report by Dr. Naylor re: Attendance at the XVI International Congress of the World Federation of Hemophilia).

¹⁴⁷⁷ Ex. 811, Vol. 182, Part I, Tab 32, p. 163 (August 23, 1984, Medical Board Meeting, World Federation of Hemophilia).

A, NON-B HEPATITIS, AND THE DEVELOPMENT OF SIDE EFFECTS.¹⁴⁷⁸

770. At the conference, Dr. Naylor met with representatives of the CHS including Ed Gurney, Linda Laxdal, and Dr. Kaiser Ali. Dr. Naylor noted that Dr. Ali "lent strong support to the CRCS decision not to distribute heat treated concentrates at this time..."¹⁴⁷⁹ Although Dr. Ali testified that he could not specifically recall this discussion documented by Dr. Naylor¹⁴⁸⁰, Dr. Naylor's report was consistent with the position subsequently adopted by the CHS MSAC at its September 12, 1984 meeting. At that meeting heat-treated concentrates were again discussed and the MSAC again reaffirmed the stand that there was insufficient data to justify the use of heat-treated concentrate at that time.¹⁴⁸¹

771. Until the discovery of the HTLV-III virus in April 1984, it was not possible to assess the potential effectiveness of heat-treatment as a means to inactivate the AIDS virus. The CDC in Atlanta was the first to release data on the effectiveness of heat-treatment on the AIDS virus. Prior to the CDC's experiments, the international hemophilia treating community was resistant to heat-treatment. Dr. Bruce Evatt of the CDC stated:

Heat-treated clotting factor was introduced (1983). This was a very interesting time, because it was licensed and introduced into the market. But nobody would use it among the hemophilia community. There were very few people who used the heat-treated factor at that time. We came out with a kind of wishy-washy one; it was not recommended by experts in hemophilia treatment...

The reasons that were given for not using heat-treated factor was, although it had been licensed for hepatitis B, it was not very effective for hepatitis B, and it was shown that people developed hepatitis who took it shortly thereafter. So people said why spend extra money on something that doesn't even work for what it is licensed to. Besides, we don't even know that it is a virus anyway.

¹⁴⁷⁸ *Ibid*, p.164.

¹⁴⁷⁹ Ex. 758, Vol. 164, Tab 11, p. 55 (September 13, 1984, Memo from Dr. Naylor to Dr. Perrault and Dr. Davey re: Summary of an Informal Meeting held with Representatives of the Canadian Hemophilia Society on August 28, 1984).

¹⁴⁸⁰ Evidence of Dr. Kaiser Ali, Pediatrician, Hemophilia Treater, pp. 32639 - 32641.

¹⁴⁸¹ Ex. 758, Vol. 164, Tab 10 (September 12, 1984, Minutes of the MSAC of CHS Meeting).

Second of all, there were theories that any kind of heat-treatment would modify the molecules so you would get inhibitors. Certainly, that was deadly. So for this theoretical basis, it was better not to use it.¹⁴⁸²

772. As Dr. Evatt pointed out, there were also concerns amongst American hemophilia treaters about the cost of these heat-treated concentrates. Heat-treated products were double the cost of regular concentrate.¹⁴⁸³

773. In mid-1984, the CDC was able to obtain a large quantity of LAV from the Pasteur Institute in France. Dr. Evatt and other researchers at the CDC commenced research to determine whether or not heat-treatment was effective in inactivating the LAV virus. The CDC found that basic lyophilization of concentrates disabled a great deal of virus.¹⁴⁸⁴ However, work was hampered as the CDC was unable to get the heat-treatment process from the various manufacturers.¹⁴⁸⁵ The preliminary results of these early heat-treatment and lyophilization experiments were presented at the World Federation of Hemophilia meeting in Rio in August as an Ad Hoc presentation.

People were excited about this, but they wanted to see the results done by one of the commercial companies.¹⁴⁸⁶

774. Consequently, the results of the CDC studies in heat-treatment using a commercial process were not available to the public until October, 1984. Once the CDC completed these tests, Dr. Bruce Evatt met with Peter Levigne, who was Medical Director of the National

¹⁴⁸² Ex. 562, Tab 47, pp. 86-87 (*Document Brief Relating to Dr. Donald Francis, Lecture: "AIDS Epidemic and Blood Safety: Changes and Attitudes from a Historical Perspective", by Dr. Bruce Evatt*).

¹⁴⁸³ *Ibid*, p. 87.

¹⁴⁸⁴ *Ibid*, p. 88-89.

¹⁴⁸⁵ *Ibid*, p. 88.

¹⁴⁸⁶ *Ibid*, p. 89.

Hemophilia Foundation.¹⁴⁸⁷ Initially Mr. Levigne was resistant to the idea of introducing heat-treated concentrates. However, after reviewing Dr. Evatt's data, the National Hemophilia Foundation proceeded to endorse the use of heat-treated concentrates based on this preliminary data on October 13, 1984.

775. The CRCS and other parties to the blood system were uncertain as to whether to proceed in light of this preliminary evidence on the efficacy of heat-treated concentrates to disable the LAV/HTLV-III virus. Not only the CRCS, but also hemophilia treaters were ambivalent about a switch to heat-treated concentrates. As Dr. Bruce Evatt reported upon meeting Dr. Levigne:

Dr. Levigne gave me a fifteen minute lecture on the evils of heat-treatment material.¹⁴⁸⁸

776. This perspective was reflected in a letter sent by Dr. Inwood to Dr. Naylor regarding Dr. Naylor's first draft of an article entitled "Heat-treated Coagulation Factor Products" dated September 28, 1994, which was scheduled to appear in the upcoming *Hemophilia Ontario* newsletter.¹⁴⁸⁹ In a tradition of ongoing communication and consultation between the CRCS and the CHS MSAC, Dr. Naylor had provided a draft of his article to all MSAC members as well as Dr. Card, Bill Rudd and Ed Guerney on September 28, 1984.¹⁴⁹⁰ Dr. Naylor's article concluded:

¹⁴⁸⁷ *Ibid*, pp. 89-90; and

Ex. 758, Vol. 164, Tab 25 (October 13, 1984, *Hemophilia Information Exchange*, Medical Bulletin #15, Chapter Advisory #20, "Recommendations Concerning AIDS and the Treatment of Hemophilia").

¹⁴⁸⁸ Ex. 562, Tab 47, p. 89-90 (Undated, "AIDS Epidemic and Blood Safety: Changes and Attitudes from a Historical Perspective", by Dr. Bruce Evatt).

¹⁴⁸⁹ Ex. 811, Vol. 182, Part 1, Tab 36 (October 4, 1984, Letter to D.H. Naylor from Martin Inwood).

Note: This letter was carbon-copied to Dr. Card.

¹⁴⁹⁰ Ex. 758, Vol. 164, Tab 14 (September 28, 1984, Letter to Dr. Card from Dr. Naylor re: Article on Heat-treated Coagulation Factor Products).

For the present, it has been decided that heat treated concentrates should not be supplied because of the reasons mentioned above and also because of their introduction might result in preference for these products over untreated ones prepared from Canadian plasma, when there is no evidence at all that the latter are more likely to transmit disease.

Optimistically, in the near future, new technologies will be developed either to synthesize virus-free coagulation factors or to inactivate viruses in products prepared from conventional sources.

Dr. Inwood replied to Dr. Naylor on October 4, 1984 concerning his draft:

I completely agree with your comments.¹⁴⁹¹

777. As of September 1984, the CRCS and the CHS MSAC were in agreement that there was still insufficient information to support a switch to heat-treated concentrate. As Dr. Card stated at the CBC Consensus Conference presentation on heat-treatment:

The last formal meeting of our group (CHS MSAC) was on September 12th, 1984. At that time, our view was similar to that of the majority of treaters, namely that the evidence for efficacy of heat-treated was insufficient to adopt their use.¹⁴⁹²

778. Drs. Zuck and Eyster in their October 1996 article state:

The Report [IOM HIV and the Blood Supply: An Analysis of Crisis Decisionmaking] criticizes the National Hemophilia Foundation and physicians for continuing to recommend non-heat-treated AHF concentrates during 1983 and most of 1984, but it does not provide a balanced discussion of the limited supply of cryoprecipitate and the restricted availability of heat-treated AHF during that period. Neither does it adequately describe the understandable reluctance of patients whose life styles had been revolutionized by the use of AHF concentrates to revert to the use of cryoprecipitate when the AIDS incidence in 1983 was only 0.6 cases per 1000 persons with hemophilia. Finally, although cryoprecipitate was considered a safer alternative to AHF concentrates between 1979 and 1985, at the highest extremes of treatment (cumulative use of >500,000 Factor VIII units) that were typical during those

¹⁴⁹¹ Ex. 811, Vol. 182, Part I, Tab 36 (October 4, 1984, Letter to D.H. Naylor from Martin Inwood).

¹⁴⁹² Ex. 759, Vol. 165, Tab 52, p. 182 (December 10, 1984, "Heat-Treated Factor VIII Concentrates: Medical Views and Implementation Strategy", by Dr. Robert Card).

years for a person with severe hemophilia, both types of treatment were associated with high HIV seroprevalence rates.¹⁴⁹³

779. In October 1984, four events occurred which contributed to a decision to pursue the conversion to heat-treated concentrate in Canada. These events were:

- The distribution of Dr. Levy's article on Mouse Retrovirus Inactivation, dated September 29, 1984;
- The subsequent October 13, 1984 recommendation of NHF MSAC;
- The information received by Mr. Craig Anhorn at the AABB conference in San Antonio, Texas on October 20 - 24, 1984; and
- The information received by the CRCS on October 26, 1984 from Dr. Poon regarding his visit to the CDC on October 15, 1984;

780. On September 29, 1984, the *Lancet* published the seminal article by Dr. Levy of the University of California School of Medicine, outlining "preliminary communication" on viral inactivation. Dr. Levy's study, which evaluated the Cutter process, was the first to assess the impact of commercial heat-treatment on a retrovirus. Although his study utilized a mouse retrovirus and not HTLV-III, it was thought that the two had similar characteristics. His study showed that prolonged heating of concentrate (68°C for 72 hours) inactivated the mouse retrovirus. This suggested that the adoption of a heating step may result in a concentrate free of infectious viruses.¹⁴⁹⁴

781. Accordingly, on October 13, 1984 the NHF revised its recommendations on AIDS and the treatment of hemophilia. In its Medical Advisory Bulletin, the NHF noted that available data, although preliminary, did suggest that the AIDS virus was heat sensitive and that hemophilia treaters should strongly consider changing to heat-treated concentrate:

¹⁴⁹³ Ex. 1299, p. 230 (Zuck and Eyster, "Blood safety decisions, 1982 to 1986: perceptions and misconceptions", *Transfusion* October 1996).

¹⁴⁹⁴ Ex. 758, Vol. 164, Tab 35, p. 152 (Jay Levy et al. "Recovery and Inactivation of Infectious Retroviruses from Factor VIII Concentrates", *The Lancet*, September 29, 1984).

We do not yet have sufficient data of scientific nature to know with certainty that viral attenuated (heat-treated) coagulation factor concentrates should now be universally adopted. However, very preliminary data do suggest that HTLV-III is heat sensitive ... Because heat-treated products appear to have no increase in untoward effects attributable to the heat-treatment, we now recommend that treaters using coagulation factor concentrates should strongly consider changing to heat-treated products with the understanding the protection against AIDS is yet to be proven.¹⁴⁹⁵

782. At an October 20 - 24, 1984 AABB Conference, a special session was held on heat-treatment in response to Dr. Levy's *Lancet* article. Conference presenters confirmed that experiments demonstrated that the AIDS virus could be killed with heat without diminishing the concentrate's effectiveness. In attendance were, *inter alia*, Mr. Craig Anhorn, CRCS Products Manager, representatives from the CCBC, the American Red Cross, and numerous AABB blood bankers.¹⁴⁹⁶

783. On October 15, 1984, Dr. Man-Chiu Poon attended the CDC and observed the studies which evaluated the Cutter process. The CDC studies showed that the AIDS virus could be killed by a heating process with minimum loss of yield. This was critically important information and provided impetus to adopt heat-treated AHF.¹⁴⁹⁷

784. Despite evidence presented by Cutter as to the development of neo-antigens, the BoB was not yet entirely satisfied as to the safety of Cutter's heat-treated concentrate. On October 22, 1984, Dr. Wark Boucher of the BoB contacted Cutter Laboratories concerning the product monograph for its soon to be licensed Cutter heat-treated Factor VIII. The BoB suggested that the product monograph contain a statement that the heating process did not result in the formation of neo-antigens. However, Cutter stated that there was no accepted test to date to detect the development of neo-antigens. Accordingly, since there was no absolute way to rule

¹⁴⁹⁵ Ex. 758, Vol. 164, Tab 25 (October 13, 1984, *Hemophilia Information Exchange - AIDS Update Medical Bulletin #15 - Chapter Advisory #20*).

¹⁴⁹⁶ Ex. 758, Vol. 164, Tab 20 (October 10, 1984, *Memo from Dr. Naylor to File re: BC AIDS Inquest - Communication from CHS*).

¹⁴⁹⁷ Evidence of Dr. Poon, Deputy Medical Director, Calgary Centre, pp. 34456 - 34457.

out the development of neo-antigens in the heat-treated process, they were hesitant to insert such a statement in the product monograph.¹⁴⁹⁸

785. On October 26, 1984, the CRCS received a letter from Dr. Poon outlining the new developments and information urging the CRCS to carefully and objectively review the issue of heat-treatment. Dr. Poon testified that the CDC studies were the turning point in the debate about whether to utilize heat-treated concentrate:

DR. POON: The whole year we are talking about whether to use heat-treated product, or non-heat-treated product, and there is now proof that, number one, it is effective, and number two, the potency is quite good. There is still ... a question as to whether it may cause inhibitor problem, but the urgency of the problem with HIV infection and having data that in fact the process is good in terms of killing the virus; ...¹⁴⁹⁹

786. The day after receiving Dr. Poon's letter, Dr. Naylor met with Dr. Card (then Chair of the CHS MSAC) to discuss recent heat-treatment developments. Dr. Card felt that a meeting between the CRCS BTS and the CHS MSAC would assist in making a decision about whether to adopt heat-treated concentrate. Dr. Naylor recognized that any move to implement heat-treated concentrate would impact on and require the cooperation of various interested parties, and as such, recommended a meeting with broader participation including representatives from the CBC, the CRCS, the CHS, the plasma fractionators, the regulators, and NAC AIDS. Dr. Card and Dr. Naylor agreed that a joint meeting with those various parties would be an effective means to obtain a consensus decision on the future of heat-treated concentrate.¹⁵⁰⁰

¹⁴⁹⁸ Ex. 998, Vol. 244, Tab 24 (October 22, 1984, Telephone Record, Cutter's Heat-Treated Factor VIII).

¹⁴⁹⁹ Evidence of Dr. Poon, Calgary Centre Deputy Medical Director, pp. 34461 - 34462.

¹⁵⁰⁰ Ex. 629, CRC Vol. 26, Tab 18 (October 29, 1984, Memo from Dr. Naylor to File re: Heat-Treated Coagulation Factor Products - Discussion with Dr. Card).

3) Consensus Conference on Heat-Treatment of Factor VIII and IX

a) **Genesis of Consensus Conference**

787. The conference proposed by Dr. Naylor during his meeting with Dr. Card was the genesis of the Consensus Conference on heat treatment of Factor VIII and Factor IX that took place on December 10, 1984. The CRCS recognized the importance of such a conference if it was to persuade the CBC to authorize the switch to heat-treated concentrate.¹⁹⁰¹

788. The switch to heat-treated concentrate might be interpreted by some as offending the self-sufficiency principle since no Canadian fractionators had the capacity or license to heat treat. The CRCS would have to contract with American fractionators. The CRCS knew that such a move would likely have a profound impact on the ability of CLL, the Winnipeg Rh Institute, and the Institut de Armand-Frappier to develop their own heat treatment processes. In addition, as the cost of heat-treated concentrates was higher and resulted in reduced yield, additional plasma collection costs would be incurred. The CRCS was mindful of its experience with the CBC over the VAX computer and the dispute over the future of fractionation in Canada. All of these factors underscored the need to provide its funder with full and complete justification for an undertaking with significant budget and political implications.¹⁹⁰² According to Dr. Perrault it would have been a "hard sell".

789. On October 29, 1984, Drs. Naylor and Derrick wrote a memo to Dr. Perrault about the recent developments in heat-treated concentrates. After outlining the recent scientific developments, they noted that a decision on the Request for Proposal for supplementary

¹⁹⁰¹ *Evidence of Dr. Perrault, former National Director BTS, pp.30780 - 30781.*

¹⁹⁰² *Ibid; and*

See also Section I B of this document.

purchases had to be made by late November. Consequently, certain problems had to be addressed "without delay":

- (i) whether, on the basis of current evidence, heat-treated product was to be introduced in Canada;
- (ii) if heated Factor VIII was to be introduced, how it would be distributed;
- (iii) and the status of the fractionation contracts, as the Canadian fractionators did not have a heat-treatment process.¹⁵⁰³

790. They suggested that the best way to resolve these issues would be to call a:

...consensus type conference to deal with these matters involving... representatives of the Canadian Blood Committee, the Canadian Medical Scientific Advisory Committee of the Canadian Hemophilia Society, the National Advisory Committee on AIDS, the Canadian Red Cross Society Blood Transfusion Service and the plasma fractionators...¹⁵⁰⁴

791. The next day, October 30, 1984, Dr. Perrault raised the issue of heat-treated concentrates during a meeting of the CBC Advisory Subcommittee. In an effort to provide members with the most up-to-date information, Dr. Perrault tabled copies of Drs. Derrick and Naylor's October 29, 1984 memo including copies of Dr. Levy's *Lancet* article and Dr. Poon's October, 1984 report on the CDC studies. Although during their testimony committee members Drs. Koopman and Langley agreed with Commission counsel's suggestion that this information was not provided, a handwritten notation at the bottom of Dr. Perrault's copy of the Derrick/Naylor memo clearly states that this information was tabled at this CBC Advisory

¹⁵⁰³ Ex. 629, Vol. 26, Tab 17, p. 96771 (October 29, 1984, Memo from Drs. Derrick and Naylor to Dr. Perrault).

¹⁵⁰⁴ *Ibid*, p. 96768.

Subcommittee meeting.¹⁵⁰⁵ A subsequent CRCS trip report¹⁵⁰⁶ and a LCDC internal memo¹⁵⁰⁷ also confirmed this.

792. Dr. Perrault provided other information including the following:

- Four U.S. fractionators had oriented their production towards heat-treated concentrate, however, only one of them was licensed in Canada;
- There was presently enough Factor VIII (non-heat-treated) at CRCS national office and in the CRCS Blood Centres, to supply Canadian hemophiliacs for two months;
- There were a further 8 million units of Factor VIII (non-heat-treated) in the production pipeline.

793. The minutes indicated that after a lengthy discussion, all members of the CBC Advisory Subcommittee approved a motion drafted in almost identical language to the recommendation set out in the Derrick/Naylor October 29, 1984 memo. The approved motion read as follows:

A MOTION WAS PROPOSED BY DR. BOWMAN AND SECONDED BY MR. COSSETTE THAT a) "A CONSENSUS TYPE CONFERENCE TO DEAL WITH HEAT-TREATED FACTOR VIII AND INVOLVING REPRESENTATIVES OF THE CANADIAN BLOOD COMMITTEE, THE CANADIAN HEMOPHILIA SOCIETY (EXECUTIVE OR MEDICAL/SCIENTIFIC ADVISORY COMMITTEE), THE NATIONAL ADVISORY COMMITTEE ON AIDS, THE CRC-BTS AND THE PLASMA

¹⁵⁰⁵ Evidence of Drs. Koopman and Langley, former CBC Advisory Subcommittee members, pp. 36357, 36361, 36364; and

Ex. 629, Vol. 26, Tab 17, p. 96766 (October 29, 1984, Memo from Drs. Derrick and Naylor to Dr. Perrault).

¹⁵⁰⁶ Ex. 629, Vol. 26, Tab 22 (November 13, 1984, Memo from Dr. Perrault to File re: CBC Advisory Subcommittee Meeting October 30, 1984).

¹⁵⁰⁷ Ex. 998, Vol 244, Tab 34, (October 31, 1984, memo from Dr. Jessamine to Director General, LCDC).

FRACTIONATORS BE HELD, AND b) THAT IT BE HELD AT THE EARLIEST OPPORTUNITY ¹⁵⁰⁸

794. In mid-November, 1984, Dr. Card wrote to all MSAC members of the CHS stating that he had reviewed the NHF MSAC recommendations of October 13, 1984, concerning the switch to heat-treated concentrates. Dr. Card reported:

As you can see from the recommendations the key words are that treaters "should strongly consider changing" but that protection is "yet to be proven". ¹⁵⁰⁹

795. Dr. Card further reported that he had discussed these recommendations with Dr. Levigne from the NHF as well as a number of treaters and physicians who attended the recent AABB meetings:

Things are changing quickly and a number of decisions may be made over the next few weeks. Because of that I would appreciate it if you could review the enclosed material and send to me any comments that you may have regarding the status of heat treated products at the present time. In addition, if you have received any further information regarding this problem, please let me know.

As I have said, the situation may change rapidly.

I will keep you informed. ¹⁵¹⁰

796. It was anticipated that a Consensus Conference would allow hemophilia treatment physicians, the CRCS and all parties in the blood system to review the pros and cons of switching to heat-treated concentrates to determine whether or not the Canadian supply in total should be switched over to exclusive use of heat-treated products.

¹⁵⁰⁸ Ex. 629, Vol. 26, Tab 21, p. 17662 (October 30, 1984, Minutes CBC Advisory Subcommittee); and

Ex. 629, Vol. 26, Tab 22 (November 13, 1984, Dr. Perrault's Memo to file re. CBC Advisory Subcommittee meeting).

¹⁵⁰⁹ Ex. 811, Vol. 182, Part I, Tab 39 (November 14, 1984, Memo to all MSAC Members from Dr. Card).

¹⁵¹⁰ Ibid, p. 190.

797. At the Executive Committee meeting of the CBC, held November 22, 1984, Dr. Don Ingraham relayed CHS requests for information concerning the adoption of heat-treated concentrates.

...without advocating the use of heat-treated Factor VIII, the Society is interested to know if clinical data is supportive of the heat-treated product to minimize the risk of viral infection. In the United States, the American Hemophilia Society recommended the use of heat-treated product.¹⁵¹¹

b) Importance of Three-Month Inventory

798. Throughout 1982, 1983 and 1984, the CRCS was faced with severe shortages of concentrate.¹⁵¹² The problem had become so acute certain surgical procedures were cancelled.¹⁵¹³ For example, in British Columbia, Dr. Growe reported in October, 1984 that for the past year and a half there had been virtually no surgery on hemophiliacs save for two emergency procedures.¹⁵¹⁴

799. In order to help alleviate a recurring problem of concentrate shortages, the CHS lobbied vigorously for a requirement that the CRCS maintain a larger reserve of product¹⁵¹⁵ The CHS executive went so far as to pass a motion calling for legal action if the situation were

¹⁵¹¹ Ex. 999, Vol. 245, Tab 8, p.1 (November 22, 1984, *Record of Decisions of Meeting of the Executive Committee of the Canadian Blood Committee*).

¹⁵¹² Evidence of Dr. Davey, former Assistant National Director BTS and Dr. Perrault, former National Director BTS, p. 26502.

¹⁵¹³ Ibid.

¹⁵¹⁴ Ex. 758, Vol. 164, Tab 29 (letter from Dr. Growe to Dr. Card, October 19, 1984).

¹⁵¹⁵ Ex. 758, Vol 164, Tab 29 (October 19, 1984 letter from Dr. Growe to Dr. Card);

Ex. 758, Vol 164, Tab 30 (October 19, 1984 Minutes of Meeting between CRCS BTS and CHS); and

Ex. 758, Vol 164, Tab 34, (October 26, 1984, Mr. Mindell Memo).

not remedied.¹⁵¹⁶ At the October 31, 1984 meeting of the CBC Advisory Sub-Committee, the CHS brought to the attention of the sub-Committee the problem of shortages of Factor VIII.¹⁵¹⁷

Item 7 - Current Factor VIII shortages and future availability of Factor VIII and Factor IX concentrates.

17. Mr. Poyser raised the issue of shortages of Factor VIII across Canada and the quality of the product particularly in relation to AIDS. Mr. Rudd provided several examples of shortages and the different provinces and referred to the report to the Blood Resources Committee of the Canadian Hemophilia Society (CHS) dated September 11, 1984.

18. Members of the Committee attempted to identify what should be an acceptable level of inventory for Factor VIII. A comparison was made with other blood products such as Abumin and ISG for which a two-month inventory is found satisfactory. It was recognized that the unpredictability of Factor VIII, with regards to the level of utilization and the incidence of recalls, constitutes a special problem. After a first proposal for a three-month inventory,

A Motion was proposed by Mr. Poyser, seconded by Dr. Perrault, to recommend to the CBC 'to support a suitable inventory supply of Factor VIII and Factor IX concentrates, that inventory being three months or greater, and to assure long-term supply planning'. All in favour.¹⁵¹⁸

800. Maintaining a three month inventory of factor concentrate as recommended by the CBC Advisory Subcommittee was a key factor for the CRCS in planning for a smooth transition to heat-treated concentrate. As the CRCS was mindful of hemophiliacs' concerns regarding past shortages and the importance of maintaining an adequate supply of concentrate, avoiding any interruption in supply was paramount. Various documents illustrate that the CBC shared this view and that the BoB was aware of CRCS efforts to maintain a three month supply:

¹⁵¹⁶ Ex. 758, Vol. 164, Tab 34, p. 131 (October 23, 1984, Minutes of CHS Executive Committee).

¹⁵¹⁷ Ex. 629, Vol. 26, Tab 21, p. 17661 (October 30, 1984, Minutes CBC Advisory Subcommittee); and

Ex. 759, Vol. 165, Tab 5 (November 1, 1984, CHS Memo).

¹⁵¹⁸ Ex. 860, Vol. 192, Tab 2, p. 88 (October 31, 1984 Record of Decisions of the Fifth Meeting of the Advisory Sub-Committee to the Canadian Blood Committee).

- A November 8, 1984 telex from Dr. Leclerc-Chevalier to Dr. Perrault responded to the issue of availability and quality of Factor VIII raised by the Canadian Hemophilia Society at the October 30, 1984 CBC Advisory Subcommittee. Dr. Leclerc-Chevalier reported that after consulting the CBC Executive Committee it was determined:

The BTS national office should take appropriate action to purchase additional Factor VIII to satisfy the needs of the Canadian population and *to keep the inventory at an acceptable level.*¹⁵¹⁹ [Emphasis added]

- A November 13, 1984 memo from Dr. Perrault to file reported on Dr. Leclerc-Chevalier's telex clarifying that it was previously established at the October 30, 1984 CBC Advisory Subcommittee that an "acceptable level" of inventory was three months or more.¹⁵²⁰
- A November 12, 1984 memo from Dr. Davey to file reported on Dr. Davey's discussion with Dr. Boucher of the BoB. Dr. Davey advised Dr. Boucher that the CRCS would be maintaining at least three months supply of Factor VIII.¹⁵²¹
- The November 22, 1984 minutes of the CBC Executive Committee noted the CHS recommendation for maintaining a three month inventory of Factor VIII and its concern regarding maintaining an adequate supply:¹⁵²²

A telephone conference was set up to permit Dr. Don Ingraham to present the item (on request from the Canadian Hemophilia Society for heat-treated Factor VIII). He recalled that at the meeting of the Advisory Sub-Committee to the CBC... the Canadian Hemophilia Society (CHS) raised the issue of the availability and quality of Factor VIII in Canada. Members of the Society are concerned with product recalls, shortages of AHF concentrates, cases where

¹⁵¹⁹ Ex. 629, Vol. 26, Tab 32 (November 8, 1984, Telex Dr. Leclerc-Chevalier to Dr. Perrault).

¹⁵²⁰ Ex. 630, Vol. 27, Tab 1 (November 13, 1984, Memo from Dr. Perrault to File).

¹⁵²¹ Ex. 629, Vol. 26, Tab 34 (November 12, 1984, Memo from Dr. Davey to File).

¹⁵²² Ex. 860, Vol. 192, Tab 3, p. 93 (November 22, 1984, Minutes of CBC Executive Committee).

elective surgery is postponed, reduced allotments of products, and in some cases, obligation to change from dried concentrates to cryoprecipitate.¹⁵²³

801. Dr. Leclerc-Chevalier's November 8, 1984 telex directing the CRCS to maintain an acceptable level of inventory was distributed at the CBC Executive Committee meeting. There was no indication in the minutes of any opposition to the CHS request for a three month inventory. Both Dr. Furesz and Boucher from the BoB attended this meeting.¹⁵²⁴

c) **CRCS Action Pre-November 16, 1984 BoB Directive**

802. Following the October 30, 1984 CBC Advisory Subcommittee meeting and before the November 16, 1984 BoB directive requiring a switch to heat-treated concentrate, the CRCS took the following action:

- a) Dr. Naylor recalled and modified the article on heat-treated concentrates which was scheduled for publication in Hemophilia Ontario. The modifications reflected the new information obtained during the month of October.¹⁵²⁵
- b) On October 31, 1984, the CRCS wrote to various fractionators and withdrew its Request for Proposal that did not specify heat-treated concentrate (a modified Request for Proposal specifying heat-treated concentrate was subsequently issued in December, 1984).¹⁵²⁶

¹⁵²³ Ex. 999, Vol. 245, Tab 8 (November 22, 1984, *Record of Decisions Meeting of the Executive Committee of the Canadian Blood Committee*).

¹⁵²⁴ Ex. 629, Vol. 26, Tab 21, p. 17661 (October 30, 1984, *Minutes CBC Advisory Subcommittee*).

¹⁵²⁵ Ex. 629, Vol. 26, Tab 17, p. 504221 (October 29, 1984 *Memo to Dr. Derrick and Dr. Naylor re: Heat-treated Factor VIII Concentrate*).

¹⁵²⁶ Ex. 629, Vol. 26, Tab 24 (October 31, 1984, *Letters from CRCS to Armour, Cutter, Connaught and Fenwal (Hyland)*); and

Ex. 942, CRCS RFP #006-84.

c) In concert with the CBC Secretariat, the CRCS began planning for the Consensus Conference. It drafted a background paper outlining the reasons for the conference including a list of suggested conference participants and a tentative agenda to be sent to potential conference participants. The CRCS emphasized the pressing need for this conference and suggested that the conference be held no later than mid-December.¹⁵²⁷ This information was subsequently provided to the CBC on November 15, 1984. The proposed invitation list drafted by the CRCS was quite broad in order to involve both Canadian and American experts. The CRCS suggested that the consensus panel members included the following¹⁵²⁸:

- Dr. D. Aaronson, Director, Coagulation Branch, Division of Blood and Blood Products, Bethesda, Maryland;
- Dr. A. Clayton, Director General, Laboratory Centre for Disease Control, Ottawa;
- Dr. N. Gilmore, Chairman, National Advisory Committee on AIDS, Montreal;
- Dr. B. Horowitz, Director of Research & Development, Blood Derivatives Program, New York Blood Centre Inc., New York;
- Dr. Richard Mathias, Consultant Epidemiologist, Ministry of Health, Vancouver;
- Dr. Stanley E. Read, Dept. of Infectious Diseases, Hospital for Sick Children, Toronto;
- Dr. R.K. Smiley, Professor and Chairman, Department of Medicine, Ottawa General Hospital, Ottawa;
- A legal nominee; and
- A concerned general public nominee(s).

¹⁵²⁷ Ex. 629, Vol. 26, Tab 25 (October 31, 1984, Memo from Dr. Derrick to File re: CRCS BTS Action Required with Reference to Organizing a Canadian Blood Committee Consensus Conference on Heat-Treated Factor VIII Concentrate).

¹⁵²⁸ Ex. 630, Vol. 27, Tab 4 (November 15, 1984, Letter from Dr. Perrault to Dr. Leclerc-Chevalier enclosing Consensus Conference Materials).

The CRCS also proposed inviting the following as participants:

- The Canadian Red Cross Blood Transfusion Service;
- The Canadian Hemophilia Society, Medical Scientific Advisory Committee;
- Connaught Laboratories Limited;
- Armour Canada Inc.;
- Baxter Travenol of Canada (Canadian Agent; Hyland Laboratories);
- Cutter Laboratories Limited;
- Alpha Therapeutics; and
- Winnipeg Rh Institute.

and the following invited observers:

- The Bureau of Biologics, Health Protection Branch, Health and Welfare Canada;
- Canadian Hemophilia Society (Lay Executive); and
- Members of Special interest Groups who may apply for admission as observers
i.e. Press.

Despite the CRCS recommendation to include all major American fractionators, the CBC did not invite the American fractionators to the conference. The reason for their exclusion is not detailed in the CBC minutes¹⁵²⁹, nor was there any satisfactory explanation given in evidence.

- d) In the two weeks following the CBC-MSAC meeting of October 31, 1984, Craig Anhorn contacted plasma fractionators and inquired about the availability of heat-treated and non-heat-treated Factor VIII. The fractionators informed him that they had non-heat-treated concentrate but that heat-treated concentrate was not available for immediate purchase.¹⁵³⁰

¹⁵²⁹ Ex. 860, Vol. 192, Tab 3, p. 12225 (November 22, 1984, Minutes CBC Executive Committee).

¹⁵³⁰ Evidence of Dr. Craig Anhorn, former Blood Products Manager CRC BTS, pp. 39180 - 39181.

- e) The CRCS kept abreast of developing information on heat-treatment. At the November 2, 1984 CRCS BTS Advisory Committee Meeting, Dr. Derrick reported on the inactivation of retroviruses in plasma noting that loss of yield was not expected to exceed 10%. In attendance at that meeting were, *inter alia*, Dr. Rivard, Dr. Clayton of the LCDC and Dr. Leclerc-Chevalier of the CBC.¹⁵³¹
- f) The CRCS maintained frequent contact with the CBC and provided ongoing information regarding heat-treated concentrates and the Consensus Conference.¹⁵³²
- g) The CRCS monitored consultations which were being held between the BoB and the OoB in the United States regarding the licensing of heat-treated concentrate.¹⁵³³
- h) On November 2, 1984, the CRCS informed Cutter that it would send an interim request for 3 - 5 million units of heat-treated AHF on a "spot" purchase basis. A spot market space was not a purchase of concentrate "off the shelf". It referred to concentrate derived from small amounts of commercial plasma that was sometimes available as a result of a fractionator's excess manufacturing capacity. If available, spot market concentrate could be purchased on a short to medium term basis, although the quantity of units available for purchase was usually quite small.¹⁵³⁴ While the CRCS was told that there was no heat-treated Factor VIII available for immediate delivery, delivery of

¹⁵³¹ Ex. 629, Vol. 26, Tab 27 pp. 73341-73342 (November 2, 1984, Minutes of the National Advisory Committee, BTS).

¹⁵³² Ex. 629, Vol. 26, Tab 32 (November 8, 1984, Telex from Dr. Denise Leclerc-Chevalier to Dr. Perrault);

Ex. 630, Vol. 27, Tab 1 (November 13, 1984, Memo from Dr. Perrault to File); and

Ex. 630, Vol. 27, Tab 8 (November 16, 1984, Telex from Craig Anhorn to Dr. Leclerc-Chevalier).

¹⁵³³ Ex. 630, Vol. 27, Tab 1 (November 13, 1984, Memo from Dr. Perrault to File); and

Ex. 629, Vol. 26, Tab 34 (November 12, 1984, Memo from Dr. Davey to File).

¹⁵³⁴ Evidence of Dr. Perrault, former National Director BTS, and Evidence of Dr. Davey, former Assistant National Director BTS, pp. 26694 - 26701.

Cutter "spot" purchase could be expected by February 1985. It was hoped that this would last until April 1985, when the earliest delivery of heat-treated factor concentrate from CRCS plasma could be expected.¹⁵³⁵

d) **CRCS Action: Post-November 16, 1984 BoB Directive**

803. On November 16, 1984, the BoB issued a telex to the CRCS, mandating a switch to heat-treated concentrates as soon as possible:

Because heat-treatment of anti-hemophilic factor, human, dried (AHF) product has been shown to inactivate some viral agents that may cause serious disease, further reliance on AHF products that have not been heat-treated cannot be justified.

The Bureau of Biologics therefore recommends the use of untreated AHF be replace as soon as possible with AHF products which have been heat-treated.¹⁵³⁶

804. The CRCS supported the BoB's directive as it could enable the CRCS to move more quickly toward the supply of heat-treated concentrate. Dr. Furesz of the BoB testified that the BoB directive was a source of relief for the CRCS:

¹⁵³⁵ Ex. 933, Vol. 230, Tab 12 (November 2, 1984, Cutter Memo); and

Evidence of Craig Anhorn, former Blood Products Manager CRC BTS, pp. 39278 - 39279.

¹⁵³⁶ Ex. 630, Vol. 27, Tab 9 (November 16, 1984, Telex from Dr. Pope); and

Ex. 999, Vol. 245, Tab 1 (November 16, 1984, Memo from Dr. Pope to Dr. Leclerc-Chevalier).

DR. FURESZ: The Canadian Red Cross also, as well as the CBC, also expressed their, may I use a word, "relief" that we made the decision so we can go ahead now and how to do it as quickly as possible.¹⁵³⁷

805. At the time of the BoB directive, both Hyland and Cutter had heat-treated Factor VIII preparations. However, only Cutter's process demonstrated effectiveness eliminating HTLV-III and was the only heated Factor VIII concentrate licensed in Canada at the time of the Consensus Conference.¹⁵³⁸ The BoB made it clear that all other fractionators would have to provide evidence of HTLV-III inactivation.¹⁵³⁹ The CRCS knew that until Hyland or any other fractionator could produce data to satisfy the BoB's criteria, Cutter would be the only supplier of heat-treated concentrate for Canadian hemophiliacs.

806. After the BoB directive was issued, the role of the Consensus Conference changed. The issue was no longer whether heat-treated concentrates would be distributed in Canada. Rather, the issue became when and how this conversion would occur. The CRCS was anxious to proceed immediately to supply heat-treated concentrates. This urgency was underscored at the November 22, 1984, meeting of the CBC Executive Committee.

¹⁵³⁷ Evidence of Dr. Furesz, BoB Panel, pp. 43105 - 43106; and

Ex. 860, Vol. 192, Tab 5, p. 158 (January 14, 1985 Minutes of the CBC Executive Committee Meeting).

Not everyone necessarily shared this view. At the January 14, 1985 meeting of the CBC Executive Committee, Dr. Bill Cochrane, Chairman of the Board and Chief Executive Officer of CLL, commented on the harsh economic impact that the BoB directive would have on CLL's fractionation operations. During his presentation, Dr. Cochrane suggested that the BoB's decision, though good in essence, was premature and that even the hemophiliac community was not expecting such a decision at so early a date.

¹⁵³⁸ Ex. 903, Vol. 225, Tab 20, p. 05249 (December 18, 1984, Summary Report, Consensus Conference of Heat-Treated Factor VIII); and

Ex. 999, Vol. 245, Tab 8, p. 2 (November 22, 1984, Record of Decisions Meeting of the Executive Committee of the Canadian Blood Committee).

¹⁵³⁹ Ex. 999, Vol. 245, Tab 34, p. 4 (December 10, 1984, BoB Position Paper Distributed at Consensus Conference); and

Evidence of Dr. Furesz and Dr. Boucher, BoB Panel, pp. 43110 - 43112.

Dr. Perrault suggested that, though a decision is already taken by the Bureau of Biologics, there is an urgent need for a consensus conference to discuss the implementation of the decision and to minimize its impact on the consumers, the distributors, the fractionators and the CRC-BTS.¹⁵⁴⁰

807. Following the BoB directive and prior to the December 10, 1984 Consensus Conference, the CRCS took the following action in preparation for the conversion to heat-treated concentrates:

- (i) On November 26, 1984 all fresh frozen plasma intended for CLL was diverted to Cutter. The CRCS ceased shipment to CLL pending its development of a proven heat-treatment process.¹⁵⁴¹
- (ii) On November 26, 1984, the CRCS sent telexes to Alpha, Armour, Cutter and Hyland following-up on its previous telephone requests for specific information on the availability of heat-treated concentrate. Canadian fractionators also received a copy of the telex and were subsequently contacted by telephone.¹⁵⁴² Replies were requested by December 5, 1984 so that the most up to date information could be presented at the Consensus Conference. The information requested is set out below:

Reference our telephone conversation concerning Factor VIII concentrate, Factor IX complex, heat-treated.

The following questions are being addressed by the Canadian Red Cross to all potential fractionators and/or suppliers or supplementary purchases for presentation to the Canadian Blood Committee conference of 12 December 1984.

Are you offering Factor VIII concentrate heat-treated. If so, please outline.

1. License Status: U.S. - Canada?

¹⁵⁴⁰ Ex. 999, Vol. 245, Tab 8, p. 3 (November 22, 1984, Meeting of the Executive Committee of the Canadian Blood Committee).

¹⁵⁴¹ Ex. 630, Vol. 27, Tab 26 (November 26, 1984, Letter from Dr. Davey to CLL).

¹⁵⁴² Ex. 903, Vol. 225, Tab 10 (December 10, 1984, Memo to Distribution from Dr. Walcroft).

2. Method of heat-treatment. Background of evidence Re: Effectiveness and Efficacy.
3. Availability of facilities for fractionation:
 - when
 - quantity
 - costs incurred
 - effects on product yields.
4. Availability of products for purchase and distribution by CRC BTS:
 - when
 - quantity
 - price (i.e. anticipated impact of heat-treatment on cost of product).¹⁵⁴³

- (iii) On November 27, 1984, the CRCS contacted Cutter requesting that it immediately heat-treat all CRCS plasma for preparation of both Factor VIII and IX concentrates.¹⁵⁴⁴
- (iv) The CRCS continued plans to co-ordinate introduction of heat-treated concentrate and arranged meetings with various fractionators to obtain supply information. These contacts included the following:
- (a) On December 4, 1984, the CRCS met with representatives from Cutter to determine the time frame within which production of heat-treated concentrates from CRCS plasma could be implemented. The CRCS was advised that it could not expect delivery of its first shipment (spot-market purchase) of heat-treated Factor VIII before the end of April 1985.¹⁵⁴⁵ This was later than the originally

¹⁵⁴³ Ex. 630, Vol. 27, Tab 28 (November 26, 1984, Telex from Dr. Naylor to Fractionators); see also Evidence of Mr. Craig Anhorn, pp. 39193 - 39194.

¹⁵⁴⁴ Ex. 630, Vol. 27, Tab 29 (November 27, 1984, Letter from Dr. Naylor to Cutter).

¹⁵⁴⁵ Ex. 630, Vol. 27, Tab 35, p. 76150 (December 6, 1984, Memo from Dr. Naylor to File); and Evidence of Mr. Craig Anhorn, former Blood Products Manager CRC BTS, pp. 39277 - 39283.

scheduled delivery date estimated by Cutter on November 2, 1984¹⁵⁴⁶ for this product of February 1985.

(b) On December 5, 1984, the CRCS met with a representative from Hyland. The CRCS was advised that Hyland had still not completed retrovirus studies on its heat-treatment process and could offer no evidence that Hemophil-T would inactivate either HTLV-III or LAV. The CRCS was also advised that due to increasing demand for heat-treated Factor VIII, Hyland could make no guarantee that its product would be available on short notice. Hyland had limited surplus fractionation capacity. Mr. Craig Anhorn testified that based on his discussion with the Hyland representative there was no product available to the CRCS on a spot purchase basis.¹⁵⁴⁷

(c) On December 5, 1984 the CRCS met with representatives of Armour, whose heat-treatment process was being assessed by the CDC and FDA. Armour's heat-treated concentrate was not licensed in Canada but it was anticipated that it would be licensed by the end of January 1985.¹⁵⁴⁸

(v) The CRCS maintained regular contact with Canadian fractionators about their ability to develop a licensed heat-treatment process or acquire already licensed technology.¹⁵⁴⁹

¹⁵⁴⁶ See paragraph 3(c) of this section.

¹⁵⁴⁷ Ex. 630, Vol. 27, Tab 37, p. 504221 (December 6, 1984, Memo from Dr. Naylor to File);

Evidence of Mr. Craig Anhorn, former Blood Products Manager, CRC BTS, pp. 39282 - 39287; and

Evidence of Dr. Davey, former Assistant National Director BTS, p. 26713.

¹⁵⁴⁸ Ex. 630, Vol. 27, Tab 38, p. 76144 (December 6, 1984, Memo to File from Dr. Naylor); and

Evidence of Mr. Craig Anhorn, former Blood Products Manager, CRC BTS, pp. 29274-29275.

¹⁵⁴⁹ Ex. 630, Vol. 27, Tab 40 (December 6, 1984, Memo from Dr. Naylor to File re: Timing of Connaught Production of Heat-treated Coagulation Factor Products);

e) **Consensus Conference Presentations and Recommendations**

808. On December 10, 1984 the Consensus Conference was held in Toronto with representatives from the CBC, the CRCS, the BoB, NACAIDS, the CHS, the CHS MSAC, the Canadian fractionators, and the CBC Advisory Subcommittee.¹⁵⁵⁰ The CRCS had recommended that American fractionators producing heat-treated AHF be invited to the Consensus Conference.¹⁵⁵¹ The executive committee of the CBC met on November 22, 1984 to discuss the Consensus Conference. The members of the CBC decided only to invite Canadian fractionators to the conference. The organization of this conference was left to the executive director of the CBC, Dr. Leclerc-Chevalier.¹⁵⁵²

809. In the presentations by the CRCS at the conference, Drs. Perrault, Davey and Naylor all stressed the need and desire to implement the switch to heat-treated concentrates as soon as possible.¹⁵⁵³ One of the key themes that surfaced throughout the conference was the complexity involved in implementing a plan that ensured a continuing supply of factor concentrates on a national basis. In his presentation, Dr. Card, Chair of the CHS MSAC, made this quite clear:

Ex. 630, Vol. 27, Tab 42 (December 7, 1984, Memo from Dr. Naylor to File re: Institute Armand Frappier); and

Ex. 630, Vol. 27, Tab 43 (December 7, 1984, Memo from Dr. Naylor to File re: RH Institute).

¹⁵⁵⁰ *Ex. 999, Vol. 245, Tab 47 (December 10, 1984, Briefing Notes for the Minister on the Introduction in Canada of Heat-Treated Factor VIII for Treatment of Canadian Hemophiliacs).*

¹⁵⁵¹ *Ex. 630, Vol. 27, Tab 4 (November 15, 1984, letter from Dr. Perrault to Dr. Leclerc-Chevalier enclosing Consensus Conference materials).*

¹⁵⁵² *Ex. 999, Vol. 245, Tab 8, p. 4 (Record of Decisions of the Executive Committee of the Canadian Blood Committee, November 22, 1987).*

¹⁵⁵³ *Ex. 631, Vol. 28, Tab 1 (December 10, 1984, Presentations of Drs. Perrault, Davey and Naylor).*

Neither the physicians nor the hemophiliacs whom I represent would tolerate a situation where portions of the country would have heat-treated products and others would not. Thus we anticipate a uniform implementation strategy.¹⁵⁵⁴

810. In outlining the plan of the CRCS for implementation, reference was made to the many factors outside the control of the CRCS, which would affect the timing of the distribution of heat-treated factor concentrates. The complex logistics of ensuring continuity of supply posed a particular challenge for the CRCS and was dependant on:

- Fractionation capacity and obtaining appropriate quantities of factor concentrates from supplementary purchases;
- Suppliers meeting delivery commitments;
- Minimizing the additional processing time required to heat-treat concentrate;
- Obtaining expected yields from plasma;
- Timely regulatory approvals including licensing and lot release by the BoB; and
- Recalls or lot rejection by BoB.¹⁵⁵⁵

811. Based on its correspondence with the fractionators outlined above and these various factors, the CRCS advised the Consensus Conference that it would be possible to begin distributing heat-treated concentrate by May 1, 1985 and that all regions of the country would receive these products by July 1, 1985. This estimate was based on the assumption that the plasma shipped to Cutter was in process and that heat-treated concentrate from this plasma would be returned to the CRCS during April 1985. It was also hoped that supplementary supplies of heat-treated concentrate discussed above would be received in April 1985. Recent utilization

¹⁵⁵⁴ Ex. 631, Vol. 28, Tab 1 (December 10, 1984, Presentation of Dr. Card, p. 3, see also presentation of Dr. Naylor, p.1).

¹⁵⁵⁵ Ex. 631, Vol. 28, Tab 1 (December 10, 1984, Presentations of Dr. Davey, Dr. Naylor and Mr. Craig Anhorn).

data suggested that there was sufficient non-heat-treated concentrate available to ensure a continuous supply until at least May 1, 1985.¹⁵⁵⁶

812. The Consensus Conference endorsed nine recommendations.¹⁵⁵⁷ The first recommendation was that heat-treated concentrate be introduced by May 1985 with a transition period not exceeding eight weeks hereafter.¹⁵⁵⁸ It was understood that implementation would occur before May 1, 1985 only if licensed heat-treated concentrate was available in sufficient quantities to fulfil Canadian requirements.¹⁵⁵⁹

813. The Consensus Conference recommended that the criteria for the use of heat-treated and non-heat-treated concentrate during the transition period would be decided by the CHS MSAC.¹⁵⁶⁰

814. The Consensus Conference recommendations were approved by the CBC Executive Committee on December 11, 1984. At that meeting, the CBC acknowledged that the recommendations had to be implemented regardless of cost implications.¹⁵⁶¹

¹⁵⁵⁶ Ex. 631, Vol. 28, Tab 1 (December 10, 1984, Dr. Naylor Presentation); and

Evidence of Dr. Davey, former Assistant National Director BTS, and Evidence of Dr. Perrault, former National Director BTS, pp. 26700 - 26774.

¹⁵⁵⁷ Ex. 631, Vol. 38, Tab 1 (Recommendations of the Consensus Conference on Heat-Treated Factor VIII, December 10, 1984).

¹⁵⁵⁸ Ex. 631, Vol. 38, Tab 1 (Recommendations of the Consensus Conference on Heat-Treated Factor VIII, December 10, 1984).

¹⁵⁵⁹ Evidence of Dr. Koopman, former member of the CBC Advisory Committee, pp. 36637-36638.

¹⁵⁶⁰ Ex. 631, Vol. 28, Tab 1 (Recommendations of the Consensus Conference on Heat-Treated Factor VIII, December 10, 1984).

¹⁵⁶¹ Ex. 860, Vol. 192, Tab 4, pp. 149 - 154 (December 11, 1984, Minutes of CBC Executive Committee Meeting).

4) Transition to Heat-Treated Factor VIII

815. Complicating the ability of the CRCS to obtain the heat-treated product was the world-wide scarcity of heat-treated factor VIII. At Cutter Laboratories, for example, inhouse inventories depleted between the end of September, 1984 and the end of February, 1985. A number of reasons contributed to the shortage including the increased demand for heat-treated product; the increased world demand for plasma, a 13% reduction in factor VIII from the conversion to the "mega standard" and recalls on factor VIII due to AIDS.¹⁵⁶² Similarly, as early as November, 1984, Hyland had indicated that Hyland had concerns about its fractionation capacity for 1985.¹⁵⁶³

816. Following the Consensus Conference, the CRCS pressed on to execute a transition to heat-treated Factor VIII. In so doing, the CRCS overcame numerous obstacles that threatened its ability to meet the implementation schedule set by the Consensus Conference. Details of the CRCS plan and the steps it took to ensure a timely and uniform transition are set out below.

a) **Implementation Plan**

817. Immediately following the Consensus Conference, Craig Anhorn set out, in a memo to Dr. Naylor, the essence of the CRCS plan to implement a transition to heat-treated concentrate.¹⁵⁶⁴ in accordance with the Consensus Conference recommendations, heat-treated concentrate was to be introduced by May 1, 1985, it was imperative that a Request for Proposal for commercial concentrate be issued immediately. Mr. Anhorn estimated that a supplementary purchase of 35,000,000 units of heat-treated concentrate would be necessary to fulfil routine

¹⁵⁶² *Evidence of Jack Ryan, former President of Cutter Biological, p. 38781-38782.*

¹⁵⁶³ *Evidence of Mr. Larry Anderson, former Product Specialist for Fenwall Blood Products Division, pp. 39112-39113.*

¹⁵⁶⁴ *Ex. 631, Vol. 28, Tab 2 (December 11, 1984, Memo from Mr. Anhorn to Dr. Naylor re: 1985 Purchases of AHF Concentrate).*

requirements and establish a three month inventory (estimated at 11,000,000 units) as required by the CBC.

818. On December 14, 1985, only four days after the Consensus Conference, the CRCS issued a Request for Proposal for 40,000,000 units of heat-treated Factor VIII for the period April 1985 to March 1986. As noted at the Consensus Conference by Dr. Naylor, the lead time for return of product from the fractionator was 5 to 6 months following the arrival of the plasma of the fractionators.¹⁵⁶⁵ Notwithstanding the hope of the CRCS that the heat-treated Factor VIII would arrive by April, 1985, it was recognized that there were many variables which could affect the delivery date including: technical failures in processing which might involve large batches of plasma and delays in the regulatory process, such as licensing of the new product and lot release of the licensed product.¹⁵⁶⁶ Mindful of the short time frame for implementation, the CRCS stipulated that respondents' proposals and samples were to be delivered to the CRCS on or before January 11, 1985 and that vendor notification would take place by February 4, 1985.¹⁵⁶⁷ Taking into account the additional time required for heat-treatment processing, testing and regulatory release, the CRCS expected to receive the first deliveries of finished concentrate in April 1985.¹⁵⁶⁸ The Request for Proposal set out a schedule requiring an initial 10,000,000 unit delivery to arrive in April to restock CRCS inventory which was kept for emergencies or national shortages. Four 4,000,000 unit deliveries were requested to supply routine requirements between May and August 1985. Monthly deliveries of 2,000,000 units to be used in conjunction with concentrate from CRCS plasma

¹⁵⁶⁵ Ex. 631, Vol. 28, Tab 1 (December 10, 1984, Presentation of Dr. Naylor); and

Ex. 631, Vol. 28, Tab 2 (December 11, 1984 Memo from Mr. Anhorn to Dr. Naylor re: 1985 Purchases of AHF Concentrate).

¹⁵⁶⁶ Ex. 631, Vol. 28, Tab 1 (December 10, 1984, Presentation of Dr. Naylor).

¹⁵⁶⁷ Ex. 942, CRCS RFP #006-84.

¹⁵⁶⁸ Ex. 631, Vol. 28, Tab 1 (December 10, 1984, Presentation of Dr. Naylor); and

Ex. 631, Vol. 28, Tab 2 (December 11, 1984, Memo from Mr. Anhorn to Dr. Naylor re: 1985 Purchases of AHF Concentrate).

would satisfy requirements until the end of March 1986.¹⁵⁶⁹ The supplementary purchases were requested to arrive as soon as possible, in the event that Canadian-sourced concentrate presently in production at Cutter did not materialize as scheduled.

819. On December 19, 1984 the CRCS formalized its 4,000,000 unit spot purchase request from Cutter that was originally negotiated in November 1984.¹⁵⁷⁰ On January 11, 1985, Cutter formally confirmed this spot purchase with the CRCS.¹⁵⁷¹ Although this spot market purchase was delivered to Canada in February and early March, it was not released by the BoB for distribution until April 29, 1988.¹⁵⁷² In December 1984 the CRCS also confirmed its intention to extend its fractionation contract with Cutter to process Canadian plasma. Given that Cutter was the only licensed fractionator whose process was proven to inactivate the AIDS virus, the CRCS was eager to maintain a long term contract with an industry leader.¹⁵⁷³

820. The time frame for implementation under which the CRCS was operating was well known. On December 20, 1984, the CRCS and the CHS released a joint statement regarding the transition to heat-treated concentrate in Canada. The statement reiterated the Consensus

¹⁵⁶⁹ Ex. 638, Vol. 35, Tab 39 (Table 2, September 27, 1985, Craig Anhorn Position Paper re: Implementation of Heat-Treated Factor VIII and IX Distribution).

¹⁵⁷⁰ Ex. 933, Vol. 230, Tab 12 (November 2, 1984, Cutter Memo); and

Evidence of Craig Anhorn, former Blood Products Manager, CRCS BTS, pp. 39278-39279.

¹⁵⁷¹ Ex. 933, Vol. 230, Tab 41 (January 11, 1985, Letter from Cutter to CRCS).

¹⁵⁷² Evidence of Mr. Craig Anhorn, former Blood Products Manager, CRCS BTS, pp. 39278 - 39279; and

Ex. 933, Vol. 230, Tab 47 (March 5, 1985, Cutter Memo).

¹⁵⁷³ Ex. 631, Vol. 28, Tab 15 (December 21, 1984, Letter from Dr. Davey to Cutter re: December 19, 1984 Conversation About Fractionation Contract); and

Evidence of Dr. Perrault, former National Director BTS, and Dr. Davey, former Assistant National Director BTS, pp. 26702-26703.

Conference recommendation for introduction of heat-treated concentrate by May 1985 with a subsequent transition period not to exceed eight weeks.¹⁵⁷⁴

821. On January 31, 1985 the CRCS Vendor Selection Committee met to discuss the various fractionators' proposals for supplementary heat-treated concentrate. As Cutter's bid was the lowest and technical reports indicated that its product was superior to the others, Cutter's bid was accepted. However, given past shortages of Factor VIII and the inability of suppliers to guarantee delivery even under contract, the CRCS decided that it was prudent to select an additional supplier to diffuse any negative impact the U.S. market situation may have on supplies of Factor VIII in Canada. Therefore, Cutter was awarded a contract for 30,000,000 units and it was agreed that the balance (10,000,000 units) would be provided by Armour as a hedge against potential supply problems with Cutter. Armour's contract was awarded on the condition that Armour obtain a license from the BoB.^{1575, 1576}

b) Regulatory/Licensing Obstacles

822. If the scheduled delivery dates (for heat-treated concentrate from Canadian plasma and supplementary purchases) were met, introduction and full conversion to heat-treated concentrate in accordance with the Consensus Conference recommendations was possible. However, various factors outside of the control of the CRCS, including production and regulatory delays, placed this schedule in jeopardy. Firm measures taken by the CRCS helped

¹⁵⁷⁴ Ex. 631, Vol. 28, Tab 17 (December 20, 1984, CRCS/CHS Joint Statement).

¹⁵⁷⁵ Ex. 632, Vol. 29, Tab 14 (February 4, 1985, Craig Anhorn Memo to File).

¹⁵⁷⁶ Armour representatives had provided the CRCS with extensive information on the status of Armour's licensing procedures and their ongoing evaluation of their heat inactivation process. Armour's concentrate was a unique product in that no stabilizers were used in the production of Armour concentrates. As stabilizers served to insulate both the Factor VIII molecule they also served to insulate any viral protein particles, thereby necessitating longer periods of heat-treatment. Armour representatives reviewed the data which was obtained by the CBC on the inactivation of LAV in lyophilized concentrates after exposure for varying periods of time. Complete inactivation of LAV had occurred at heating for five minutes at 60°C.

to ensure heat-treated concentrates were introduced by May 1985 with full conversion by July 1985.

823. During the months leading up to the introduction of heat-treated concentrate, the CRCS continued to work with the BoB in order to expedite licensing approval and the release of heat-treated concentrate by the BoB. Some of the regulatory issues that contributed to delays in the delivery of heat-treated concentrate to the CRCS included the following:

- (a) Overlapping jurisdiction between the BoB in Canada and the OoB in the United States caused confusion when the issue of bilingual labels was raised. The CRCS could not distribute imported commercial heat-treated concentrate unless it met the dual licensing and labelling requirements of the OoB and the BoB. Each regulatory authority had different requirements which caused delay in the approval process. To allow sufficient room for both French and English information on the Canadian vial labels, the CRCS requested that certain information (manufacturer's address and license numbers) be dropped. U.S. regulations did provide for a "partial label" however the conditions under which it was permitted were not clear. In order to expedite the appropriate regulatory approval, Dr. Tom Walker of the CRCS, wrote to Dr. Boucher at the BoB on February 26, 1985 requesting that the BoB act quickly to contact Cutter and advise that the CRCS proposal for labelling satisfied Canadian regulatory requirements. Dr. Walker wrote:

There is some urgency in our request. Initial shipments of heat-treated coagulation factors derived from CRC BTS Plasma ... cannot proceed until new labelling materials are prepared.

Your efforts to resolve these matters are sincerely appreciated.¹⁵⁷⁷

¹⁵⁷⁷ Ex. 1001, Vol. 247, Tab 18, p. 2 (February 26, 1985, Letter from Dr. Tom Walker to Dr. Boucher).

- (b) The CRCS also worked with others together to expedite the release of concentrate having other labelling deficiencies. In March 1985, the CRCS confirmed with the BoB that a significant number of vials labelled without the appropriate Canadian license number or drug identification number were needed urgently and that permission to have the concentrate shipped to Canada should be treated as an emergency.¹⁵⁷⁸ In their testimony, Dr. Perrault and Dr. Davey summarized the desperate situation:

DR. DAVEY: ...The problem we sat with on March 12th ... was that Armour wasn't yet a licensed supplier.

DR. PERRAULT: And, in fact, we begged the Bureau of Biologics at that point to expedite the process, to make sure that we did meet this.¹⁵⁷⁹

- (c) Canadian licensure of Armour's heat-treated Factor VIII, which was originally expected by the end of January 1985, was not obtained until mid-April 1985.¹⁵⁸⁰

c) **Production/Supply Problems**

824. The plan to implement heat-treated concentrate as soon as possible was contingent upon a number of key assumptions including the ability of Armour and Cutter to satisfy production and delivery commitments. Details of supply problems faced by the CRCS during the Spring of 1985 are set out below:

- (a) On February 8, 1985 Cutter informed the CRCS that it would not be able to guarantee supply of the 30,000,000 unit contract. Cutter hoped to honour its

¹⁵⁷⁸ Ex. 933, Vol. 230, Tab 56 (March 25, 1985, BoB Memo to File).

¹⁵⁷⁹ Evidence of Dr. Perrault, former National Director BTS, and Evidence of Dr. Davey, former Assistant National Director BTS, p. 26789.

¹⁵⁸⁰ Ex. 978, Vol 275, Tab 33, (December 6, 1984 Memo from D. Naylor to File); and
Ex. 634, Vol. 31, Tab 18, p. 2 (April 16, 1985, Memo from Dr. Naylor to File).

supply agreement but could offer no guarantee "due to anticipated high [heat-treatment] demand and restricted supply in the market place."¹⁵⁸¹

- (b) Concerned about Cutter's inability to provide a product guarantee, Dr. Davey insisted that Cutter provide copies of its confidential inventory print outs on commercial lots destined for Canada. This represented an extraordinary concession by Cutter given the commercial sensitivity of the data but was deemed necessary by the CRCS as a means to monitor the supply of heat-treated concentrate.¹⁵⁸²
- (c) On March 11, 1985, Cutter advised the CRCS that it could not honour its delivery schedule because its inventory of heat-treated concentrate was seriously depleted due to over selling of production and poor inventory management. Delivery of Cutter's initial shipment, originally scheduled for April 1985, would be delayed until the end of June. Although Cutter was advised that this was not acceptable, the CRCS recognized that it was vulnerable and dependent upon Cutter's ability to meet its supply obligations. The CRCS was also concerned about the potential for a U.S. government embargo on the export of Factor VIII in order to maintain adequate U.S. supplies which had dwindled in the face of rising demand.¹⁵⁸³

825. Thus, by mid-March the supply situation did not look promising. Armour had not yet been licensed, and it appeared that only the Cutter/CRCS concentrate (scheduled for the end of April) would be available to commence implementation of heat-treated concentrate. On

¹⁵⁸¹ Ex. 632, Vol. 29, Tab 16 (February 8, 1985, Minutes of Cutter/CRCS Meeting).

¹⁵⁸² Ex. 933, Vol. 230, Tab 46 (February 20, 1985, Internal Cutter Memo).

¹⁵⁸³ Ex. 876, Vol. 208, Tab 44 (March 12, 1985, Memo from Dr. Tom Walker to File re: March 11, 1985 Meeting with Cutter); and

Evidence of Dr. Davey, former Assistant National Director BTS, and Evidence of Dr. Perrault, former National Director BTS, pp. 26786 - 26788.

March 20, 1985, Dr. Perrault informed the CBC about the delivery schedule crisis and noted the distinct possibility of incomplete supply due to substantially increased demand for heat-treated concentrate.¹⁵⁸⁴ In his testimony, Dr. Davey described the precarious supply situation as of mid-March 1985:

DR. DAVEY: Now, I'll tell you what resources we had ... on this afternoon, in terms of heat-treated product: none in hand; an order placed as a spot purchase in early January to Cutter for 4 million units of heat-treated AHF. This had not been delivered, we were told [in late February] that samples were at BoB for lot release and that some were coming in March, we should, at best, see the product by late March. In fact, we saw it in June. And the second supplier, still unlicensed, but scheduled to deliver products within two weeks.

So we didn't have any heat-treated AHF and we had no immediate prospect and we were quite concerned about even being able to introduce AHF on the 1st of May.¹⁵⁸⁵

Cutter's shortage was so acute that it eventually had to divert heat-treated concentrate from California's supply in order to fill the CRCS order.¹⁵⁸⁶

826. The CRCS continued to up-date its personnel and others regarding the status of implementation. On March 20, 1985, Dr. Naylor issued a memo to all CRCS Medical Directors advising them about the upcoming transition to heat-treated concentrate. He noted that there would be limited amounts of heat-treated Factor VIII and IX distributed to the Blood Centres from May 1 to July 1, 1985. During this transition period, a proportionate amount of heat-treated concentrate would be sent to each Centre, to be determined by the estimated number of eligible patients. Accordingly, Medical Directors were asked to communicate this information

¹⁵⁸⁴ Ex. 743, Tab 7, *Documents for Examination of Dr. Perrault and Dr. Davey*, (March 20, 1985, Letter from Dr. Perrault to Dr. Leclerc-Chevalier re: Supply of Factor VIII Concentrate from Cutter).

¹⁵⁸⁵ *Evidence of Dr. Davey, former Assistant National Director BTS*, pp. 26788 - 26789.

¹⁵⁸⁶ *Evidence of Dr. Davey, former Assistant National Director BTS*, p. 26790.

to hemophilia treatment centres and physicians. In addition, the memo was copied to Dr. Card and Bill Rudd, Chair of the CHS Blood Products Committee.¹⁵⁸⁷

827. On March 23, 1985, Dr. Naylor attended a meeting of the Ontario CHS MSAC and advised Committee members that the transition to heat-treated concentrates would occur according to schedule with limited amounts of product available during the transition period. The Ontario CHS MSAC drafted its criteria for the distribution of heat-treated concentrate during the transition period.¹⁵⁸⁸ It is important to note that the "priority list" which was subsequently endorsed by the National CHS MSAC and the CHS Board was drafted by experienced hemophilia treaters and not the CRCS.

828. On April 20, 1985 the Board of Directors of the CHS met and approved the following criteria, established by its MSAC, for the distribution of heat-treated product during the conversion period:

- previously untreated or rarely treated patients, who require concentrate therapy during the conversion period.
- previously treated patients known to be sero-negative for HTLV-III antibodies.
- young children who require concentrate during this period.
- those regularly treated with cryoprecipitate who require factor concentrate for isolated indications, including major surgery or travel.
- the distribution across the country to be equitable.
- the decision of priorities to be done by hemophilia clinic directors, in consultation with CRC BTS centre directors.¹⁵⁸⁹

¹⁵⁸⁷ Ex. 633, Vol. 30, Tab 7 (March 20, 1985, Memo from Dr. Naylor to Medical Directors).

¹⁵⁸⁸ Ex. 633, Vol. 30, Tab 14 (March 23, 1985, Trip Report to the Ontario CHS MSAC Annual Meeting).

¹⁵⁸⁹ Ex. 761, Vol. 167, Tab 59, p. 187 (April 20, 1985 Minutes of the Canadian Hemophilia Society Annual General Meeting and Board of Directors Meeting).

d) **Planned Inventory vs. Actual Deliveries**

829. To illustrate the uncertainty the CRCS faced in managing its heat-treated supply during the transition period, a table is set out below comparing planned inventory with actual deliveries. Following the table, there is a brief commentary summarizing significant aspects of this information¹⁵⁹⁰.

Heat-Treated Factor VIII: Planned Deliveries vs. Actual Deliveries						
<u>Date</u>	<u>Cutter Planned</u>	<u>Cutter Delivered</u>	<u>Armour Planned</u>	<u>Armour Delivered</u>	<u>Cumulative Planned</u>	<u>Cumulative Delivered</u>
April, 1985	7,500,000 4,000,000*		2,500,000			
April 25				1,635,860		
April 29		2,577,960				
Total	11,500,000	2,577,960	2,500,000	1,635,860	14,000,000	4,213,820
May, 1985	3,000,000		1,000,000			
May 1				3,590,380		
Total	3,000,000	0	1,000,000	3,590,380	18,000,000	7,804,200
June, 1985	3,000,000		1,000,000			
June 5		7,258,930				
June 13		3,723,440*				
Total	3,000,000	10,982,370	1,000,000	0	22,000,000	18,786,570
July, 1985	3,000,000		1,000,000		4,000,000	
July 5				793,450		
July 15		3,764,470				
July 26		3,835,580				
Total	3,000,000	7,600,050	1,000,000	793,450	26,000,000	27,180,070
* Heat-Treated Factor VIII Concentrate From CRCS Plasma						

¹⁵⁹⁰ Complied from Information Contained in Ex. 638, Vol. 35, Tab 39 (Tables 2 and 3, September 27, 1985. Craig Anhorn Position Paper re: Implementation of Heat-Treated Factor VIII and IX Distribution).

830. On April 25, 1985, the CRCS received its first shipment of heat-treated Factor VIII. Armour delivered approximately 1.6 million units of its recently licensed concentrate. Not only was this shipment approximately four weeks late, it was approximately 870,000 units short of the contract amount for the month of April. Cutter's first shipment of approximately 2.5 million units arrived April 29, 1985. Also late, this shipment represented a shortfall of approximately 5 million units from Cutter's supplementary contract amount for the month of April. However, given that Cutter's commitment to deliver 4 million units from CRCS plasma was delayed until June 13, Cutter's total shortfall for the month of April was approximately 8.9 million units. Overall, the CRCS plan had anticipated receipt of approximately 14 million units by the end of April. However, given the various factors cited above, only 4.2 million units were received. At the start of May 1985, the CRCS was faced with a shortfall of approximately 10 million units.¹⁵⁹¹

831. In May 1985, the gulf widened between deliveries expected and those actually received. Cutter sent no Factor VIII at all, although the CRCS did receive approximately 3.5 million units from Armour on May 1, 1985. No further shipments were received in May so that by the end of the month, the CRCS had received approximately 7.8 million units which represented a cumulative shortfall of approximately 10.2 million units.¹⁵⁹²

832. On May 15, 1985, the CRCS met with Cutter representatives and discussed *inter alia* delays with Cutter's production/delivery schedule.¹⁵⁹³ Although Cutter advised that it would likely satisfy its June delivery commitments, the ability of the CRCS to fully convert to heat-treated Factor VIII by July 1, 1985 was still contingent upon the following variables:

- Whether Cutter would in fact deliver as promised;
- If and when the Cutter/CRCS heat-treated concentrate was received;

¹⁵⁹¹ Ex. 638, Vol. 35, Tab 39 (Tables 2 and 3, September 27, 1985 Craig Anhorn Position Paper re: Implementation of Heat-Treated Factor VIII and IX Distribution).

¹⁵⁹² *Ibid.*

¹⁵⁹³ Ex. 635, Vol. 32, Tab 15 (May 15, 1985, Dr. Naylor Trip Report to Cutter in Clayton, North Carolina).

- Whether a significant number of lots were rejected or recalled by the BoB.¹⁵⁹⁴

Fortunately, Cutter met its June commitments under the supplementary purchase agreement and also delivered approximately 3.7 million units of CRCS/Cutter heat-treated concentrate. Nevertheless, cumulative deliveries by the end of June were approximately 3.2 million units less than expected. It was not until July that overall deliveries met the need for a stable supply, including the three month reserve inventory.¹⁵⁹⁵

833. It should be noted that of the 3.7 million units of concentrate from CRCS plasma that Cutter delivered on June 13, 1985, approximately 1.8 million units were defective and could not be distributed. This substantially reduced the supply of heat-treated Factor VIII available for distribution prior to the July 1, 1985 conversion date.¹⁵⁹⁶

834. The CRCS worked to overcome the various regulatory and supply problems that occurred throughout the first half of 1985. Working in conjunction with its regulators and fractionators, the CRCS satisfied the timetable for conversion that was recommended by the Consensus Conference and approved by the CBC and CHS. Despite these efforts, the CRCS has been criticized for not moving to full conversion prior to July 1, 1985. However, it was the considered opinion of the CRCS that, given what it knew at the time about the precarious state of supply, it would have been premature and irresponsible to fully convert before July 1, 1985.

¹⁵⁹⁴ Evidence of Dr. Perrault, former National Director BTS, and Evidence of Dr. Davey, former Assistant National Director BTS, pp. 29381 - 29383.

¹⁵⁹⁵ Ex. 638, Vol. 35, Tab 39 (Tables 2 and 3, September 27, 1985 Craig Anhorn Position Paper re: Implementation of Heat-Treated Factor VIII and IX Distribution).

¹⁵⁹⁶ Ex. 943, p. 5 (CRCS Stock Record Card for Cutter/CRC BTS Heat-Treated Factor VIII (Lots C8P001 and C8P002) Information contained on this Stock Record Card confirms that 7,191 vials of lot C8P001 and 100 vials of lot C8P002 were destroyed in May and June of 1986. This represented a loss of 1,893,660 units of heat-treated Factor VIII delivered by Cutter on June 13, 1985.)

The CRCS believed that attempting a full conversion any earlier without appropriate assurances for continued supply would have defeated the purpose of the conversion.¹⁵⁹⁷

835. Advancing the conversion date by distributing all heat-treated concentrate on hand, would have left the CRCS without the critical three month reserve inventory that the CHS lobbied so hard to obtain. Maintaining emergency reserves of the new heat-treated concentrate was a key factor in implementing an orderly and responsible conversion. If the CRCS had rushed the conversion date and supplies were interrupted, the results could have been disastrous. Patients who had started receiving heat-treated concentrate could have been forced to revert to non-heat-treated concentrate, clearly a situation that would have been unacceptable from both an administrative and ethical point of view.¹⁵⁹⁸ Because the bulk of the supply planned for April 1985 did not materialize until June, the CRCS struggled to build its inventory for normal distribution and was unable to establish emergency supplies for much of the transition period:

DAVEY. ...But quite clearly, if we would put ten weeks' supply out to make the complete conversion, we would need a back-up supply at National Headquarters to meet any of these, both demand for deferred procedures, and also, of course, any emergencies, any acute large needs that occurred at centres.

Now, that ten-week supply was approximately 9 million units. So certainly at the end of May, we didn't even have that in the national stock, about 7 million units there. So through June we planned to complete - to continue the restricted distribution.

In May, two or three centres had received additional stocks of heat-treated product to meet some emergency demands.

The third of June, we received approximately 8 million units from Cutter and shortly after that, the 13th of June, the first shipment of the Canadian source product which is at the foot of the page, and that stage, we reached the level at which we said national distribution should become feasible which was the order of 18 million units of Factor VIII, heat-treated factor VIII, actually delivered.

¹⁵⁹⁷ Evidence of Dr. Perrault, former National Director BTS; and Dr. Davey, former Assistant National Director BTS, pp. 26825-26826; and

Evidence of Ms. Harrington, Nurses Panel, p. 35188.

¹⁵⁹⁸ Evidence of Dr. Perrault, former National Director BTS, and Evidence of Dr. Davey, former Assistant National Director BTS, pp. 26815 - 26828; 29440 - 29441.

Now, the question was then should we advance the conversion date by what would have been approximately two weeks, make that initial 9 million units distribution and rest on the ten weeks, approx. - ten weeks, stock remaining.

Now, we had a so called 'guarantee' in May, from Cutter that they would meet their schedules. But we were aware that, first of all, the guarantee was subject to lot release and subject to no-lot failures and productions, and second: we were also vulnerable, had there been any lot withdrawal by either Cutter or Armour at this stage. And of course, the previous two years had seen a number of large withdrawals of Factor VIII because of possible contamination of plasma source. This was Factor VIII already in the field.

So quite frankly, sir, we were not prepared to advance the date. We held the original date of first of July. We did our initial major distribution in the last week of June and made the conversion as scheduled. Now, I have to note that ~~by~~ by that date, we didn't have any more. We did get some in the following week from Armour, not a very large supply.

But we felt that we had made the undertaking. We should do it. We were vulnerable to emergency demands, we were vulnerable to lot withdrawals. And in retrospect, we might as well have done this two weeks earlier, as on the first of July. Now, that is about the window of opportunity I see from this perspective.

...

...We had reached a target by the 13th of May, but had to be cautious about it in the lack of absolute guarantees that further supply, or the picture in retrospect is - one may have advanced this state by two weeks.¹⁵⁹⁹

836. There were other important reasons for establishing a reserve inventory pending adequate assurances of continued supply. They included the following:

- (a) Unexpected treatment for patients with inhibitors posed a serious risk to reserve inventories. Two or three inhibitor patients requiring ongoing massive infusions had the potential to deplete local and even national inventories.¹⁶⁰⁰
- (b) Although many hemophiliacs had deferred elective surgery and dental procedures during the transition period, utilization rates were expected to substantially

¹⁵⁹⁹ Evidence of Dr. Davey, former Assistant National Director BTS, pp. 30828-30830.

¹⁶⁰⁰ Evidence of Dr. Davey, former Assistant National Director BTS, pp. 26443 - 26444.

increase as soon as the CRCS moved to full conversion.¹⁶⁰¹ This prediction proved correct as CRCS records indicated that issues of concentrate jumped by 61 % following the July 1, 1985 conversion date.¹⁶⁰²

- (c) The CRCS also reasonably expected demand for heat-treated concentrate to increase after July 1, 1985, as hemophiliacs on home care began replenishing their stocks and other patients switched from cryoprecipitate back to concentrate.¹⁶⁰³

837. For all of the above reasons, the CRCS believed it was prudent to implement full conversion on July 1, 1985, in accordance with the Consensus Conference recommendation. Prior to that date no request or order for heat-treated concentrate was refused. There was no evidence that a single hemophiliac who was entitled to heat-treated concentrate under the MSAC guideline was refused by the CRCS.¹⁶⁰⁴ After that date, no non-heat-treated concentrate was distributed in Canada and all remaining non-heat-treated Factor VIII was withdrawn and destroyed.¹⁶⁰⁵

¹⁶⁰¹ Evidence of Dr. Perrault, former National Director BTS, p. 26791.

¹⁶⁰² Ex. 638, Vol. 35, Tab 39 (September 27, 1985, Craig Anhorn Position Paper re: Implementation of Heat-Treated Factor VIII and IX Distribution).

¹⁶⁰³ Ex. 635, Vol. 32, Tab 36 (May 30, 1985, Dr. Naylor's Memo to CRCS Medical Directors);

Evidence of Dr. Inwood, Hemophilia Treater, pp. 33731-33732;

Evidence of Dr. Gorelick, Halifax Centre Medical Director, pp. 13161-13162; and

Evidence of Ms. Roy, Laboratory Manager, St. John CRCS Centre, p. 11865.

¹⁶⁰⁴ Evidence of Ms. Roy, Laboratory Manager, New Brunswick CRCS Centre, p. 11858;

Evidence of Dr. Huntsman, Newfoundland Centre, pp. 13987-13988; and

Evidence of Drs. Davey and Perrault, p. 30803.

¹⁶⁰⁵ Ex. 638, Vol. 35, Tab 39 (Tables 3 and 5, September 27, 1985, Craig Anhorn Position Paper re: Implementation of Heat-Treated Factor VIII and IX Distribution).

e) **Local CRCS Blood Centre Distribution**

838. Although many hemophiliacs had deferred elective surgery during the transition period, the CRCS recognized that a serious accident or other trauma requiring surgery could cause severe bleeds requiring massive infusions to control.¹⁶⁰⁶ For example, in Vancouver, two hemophiliacs required urgent surgical procedures necessitating approximately 120,000 units of heat-treated concentrate, an amount almost four times greater than that used by an average hemophiliac in a single year.¹⁶⁰⁷ Dr. Teitel testified that in a surgical procedure, a hemophiliac could require as much as 100,000 units of Factor VIII.¹⁶⁰⁸ CRCS Medical Directors understood the importance of reserving heat-treated concentrate during the transition period for only those patients who satisfied the criteria of the CHS MSAC protocol. The Medical Directors were mindful that heat-treated concentrate in their Centre inventories could have been depleted by an unforeseen surgery, accident or trauma requiring vigorous treatment.¹⁶⁰⁹

839. Between April and July 1985, the CRCS rotated its inventories and provided initial shipments of heat-treated concentrate to all its Blood Centres. Each Centre received a one week supply on April 30, 1985. A further two weeks' supply followed on June 11 and then again on June 24, 1985. These steps were taken to ensure an equitable distribution and uninterrupted conversion to heat-treated concentrate.¹⁶¹⁰

¹⁶⁰⁶ *Evidence of Dr. Perrault, former National Director BTS, pp. 26440 - 26443.*

¹⁶⁰⁷ *Ex. 634, Vol. 31, Tab 35 (May 3, 1985, Memo from Dr. Buskard to Dr. Naylor); and Evidence of Dr. Davey, former Assistant National Director BTS, pp. 26443 - 26444.*

¹⁶⁰⁸ *Evidence of Dr. Teitel, Medical Director, Hemophilia Ontario, pp. 34011-34014.*

¹⁶⁰⁹ *Evidence of Dr. Schroeder, Winnipeg Centre Medical Director, pp. 10161 - 10162; Evidence of Dr. Gorelick, Halifax Centre Medical Director, pp. 12930 - 12939; and Evidence of Dr. Ross, Medical Director, Charlottetown Centre, pp. 32820 - 32822.*

¹⁶¹⁰ *Ex. 638, Vol. 35, Tab 39 (Tables 4 and 8, September 27, 1985 Craig Anhorn Position Paper re: Implementation of Heat-Treated Factor VIII and IX Distribution).*

840. Despite the pointed criticism that some CRCS Medical Directors received for failing to distribute heat-treated concentrate on hand, the CRCS was never unable or refused to fulfil an order for any doctor or hospital once heat-treated product became available. All such requests from treaters were satisfied.¹⁶¹¹

841. The decision to follow the protocol was the responsibility of the treating physicians. In Newfoundland, for example, where there existed a comprehensive hemophilia care centre, the CRCS blood centre immediately distributed almost all of its heat-treated product to the clinic as soon as it was available. The treaters decided not to follow the protocol but to give heat-treated product to all hemophiliacs who needed.¹⁶¹² The result of this policy was that the comprehensive care centre depleted its inventory of heat-treated product during the conversion period and at times was unable to distribute the heat-treated product to those patients who fit the protocol.¹⁶¹³

5) Transition to Heat-Treated Factor IX

842. Heat-treated Factor IX presented different problems for the CRCS. Unlike heat-treated Factor VIII, heat-treated Factor IX was a relatively new product. The first heat-treated Factor IX concentrates were licensed by the U.S. FDA between October 26 and 29, 1984.¹⁶¹⁴

¹⁶¹¹ Evidence of Ms. Roy, *Laboratory Manager, New Brunswick CRCS Centre*, p. 11858;

Evidence of Dr. Huntsman, *Newfoundland Centre*, pp. 13987-13988; and

Evidence of Drs. Davey and Perrault, p. 30803.

¹⁶¹² Evidence of Dr. Ali, *Newfoundland Hemophilia Treater*, p. 32667.

¹⁶¹³ Evidence of Dr. Ali, *Newfoundland Hemophilia Treater*, pp. 32687-32692.

NOTE: There is no evidence to clarify whether more heat-treated product was requested or required from the CRCS once the hemophilia care centre used up all of its heat-treated product.

¹⁶¹⁴ Ex. 556, Vol. 129, Tab 68 (December 12, 1984, *Hemophilia Information Exchange, Medical Bulletin*. "Heat-treated Factor IX Now Available").

It was only in mid-December, 1984, that the NHF recommended that hemophiliacs and hemophilia treaters adopt the use of heat-treated Factor IX concentrates.¹⁶¹⁵ There remained a concern, however, about the heat-treated Factor IX process changing the effectiveness of the prothrombin complex concentrate used to treat bleeding in patients with inhibitors.¹⁶¹⁶

There was no in vitro assay that predicts the clinical efficacy of these products when used for inhibitor patients and "factor VIII bypassing activity" may be inactivated by the heat treatment. At the present time, studies are underway at several treatment centres to evaluate the effectiveness of heat treated factor IX for the treatment of bleeding in factor VIII deficient persons with inhibitors.¹⁶¹⁷

This bulletin further stated that information on heat-treated Factor IX concentrates might not be available for a year or more.¹⁶¹⁸

843. While the CRCS moved quickly to facilitate the implementation of heat-treated Factor IX, various obstacles outside the control of the CRCS precluded the CRCS from securing a supply of heat-treated Factor IX by the proposed implementation date. Problems, including those associated with the overlapping jurisdiction of the BoB and the OoB, caused delays and prevented delivery of any heat-treated Factor IX until May 30, 1985. The steps taken by the CRCS to expedite regulatory approval and delivery are set out below.

¹⁶¹⁵ *Ibid*, p. 68.

¹⁶¹⁶ *Ibid*, p. 68.

¹⁶¹⁷ *Ibid*, p. 68.

¹⁶¹⁸ *Ibid*, p. 68.

a) **Implementation Plan**

844. Following the November 1984 BoB directive, the CRCS requested Cutter to heat treat the Factor IX lots from CRCS plasma which was already in Cutter's possession. Although the BoB directive did not specifically refer to Factor IX, in the interest of providing additional safety, the CRCS decided to interpret the directive to require a switch to heat-treated Factor IX as well.¹⁶¹⁹

845. The CRCS spoke with Cutter on various occasions between November 19 - 26, 1984 and discussed how to obtain heat-treated Factor IX as soon as possible. Unlike Factor VIII, Factor IX did not require stabilizers in order to maintain specific activity and as such, existing Factor IX could be heated "in vial" without a significant loss of yield. On November 27, 1984, the CRCS wrote to Cutter and confirmed its verbal request made the previous day for Cutter to heat treat two lots of Factor IX (C9N005 and C9N006) which were to be shipped back to the CRCS once labelling was completed. It also requested that all future lots of Factor IX be heat-treated as a matter of routine. The CRCS also requested information on the status of Cutter's Factor IX license. Although the fractionator had already received a Notice of Compliance for heat-treated Factor VIII, Cutter's heat-treated Factor IX application was still pending review by the BoB.¹⁶²⁰

846. In addition to Cutter, the CRCS also canvassed other fractionators about their ability to provide commercial heat-treated Factor IX during meetings with the U.S.

¹⁶¹⁹ Ex. 630, Vol. 27, Tab 11, p. 504221 (November 19, 1984 Memo from Dr. Naylor to File)

¹⁶²⁰ Ex. 630, Vol. 27, Tab 25 (November 26, 1984 Craig Anhorn Memo to File re. Cutter Heat-Treated Factor VIII and Factor IX); and

Ex. 630, Vol. 27, Tab 29 (November 27, 1984 Letter from Dr. Naylor to Cutter re. Heat-Treated Factor VIII and Factor IX from CRCS Plasma).

fractionators.¹⁶²¹ This was confirmed in Dr. Naylor's November 26, 1984 telex to the U.S. fractionators.¹⁶²²

847. At its December 4, 1984 meeting with Cutter, the CRCS was advised that two lots of Factor IX (approximately 10,000 vials) had been heat-treated in vial. Cutter confirmed that its licensing application for heat-treated Factor IX had been submitted to the BoB and that license approval was anticipated in January 1985.¹⁶²³ The CRCS was told that the projected release date for this product was April 1, 1985.¹⁶²⁴

848. Based on its discussions with Cutter, Dr. Davey informed delegates at the December 10th Consensus Conference:

As Factor IX can be heated without loss of potency, the use of heat treated Factor IX can be implemented sooner than Factor VIII.¹⁶²⁵

Various regulatory obstacles (outside of the control of the CRCS) delayed delivery until May 30, 1985. Details of these obstacles and the measures taken by the CRCS to address them are set out below.

¹⁶²¹ Ex. 630, Vol. 27, Tab 35 (December 6, 1984 Dr. Naylor's Memo to File re. Meeting with Cutter);

Ex. 630, Vol. 27, Tab 37 (December 6, 1984 Dr. Naylor's Memo to File re. Meeting with Hyland); and

Ex. 630, Vol. 27, Tab 38 (December 6, 1984 Dr. Naylor's Memo to File re. Meeting with Armour).

¹⁶²² Ex. 630, Vol. 27, Tab 28 (November 26, 1984 Telex from Dr. Naylor to U.S. fractionators).

¹⁶²³ Ex. 630, Vol. 27, Tab 35 (December 6, 1984 Dr. Naylor's Memo to File re. Meeting with Cutter).

¹⁶²⁴ Ex. 743, Tab 37 (January 1985 Plasma Production and Derivative Inventory Status Report for Factor IX Lots - C9N005A, C9N006A and C9P001).

¹⁶²⁵ Ex. 903, Vol. 225, Tab 20A, p. 5250 (December 18, 1984, Summary Report, Consensus Conference on Heat-Treated Factor VIII).

b) **Regulatory/Licensing Obstacles**

849. Although Factor IX, already in Cutter's possession, was heat-treated in vial by December 6, 1984,¹⁶²⁶ it had to be tested and samples had to be submitted to both the BoB and the OoB. U.S. regulations required the OoB to test, release and approve any modification of Factor IX before Cutter could export it to Canada. While one of the lots (C9N005) had previously been submitted in its non-heat-treated form, it had to be withdrawn, retested and resubmitted to the regulators after heat-treating.¹⁶²⁷

850. Mr. Jack Ryan, former President of Cutter, testified that overlapping jurisdiction between the BoB and OoB caused confusion and delayed the finalization of labelling and packaging. In addition to delay associated with approval of bilingual labelling, there was also a delay associated with U.S. regulatory approval of the label content.¹⁶²⁸ In the past, labels of Factor IX contained a list of factors present in the preparation. Changes to FDA regulations subsequently required the list of components to be deleted from the carton and vial label. As the CRCS anticipated using different types of Factor IX in the future, it wanted the list of components reflected on the packaging so that users would be able to differentiate between the various Factor IX preparations. This request was made to alleviate any future confusion caused by the US regulatory requirement. In his February 26, 1985 letter to the BoB, Dr. Tom Walker requested the BoB's assistance in order to resolve the issue with the OoB. He emphasized the urgency involved given that future shipments of heat-treated concentrate from CRCS plasma could not proceed until new labels were prepared.¹⁶²⁹

851. Despite its initial concerns, the CRCS remained hopeful that shipments of heat-treated Factor IX would be delivered on time for distribution by the May 1, 1985 introduction

¹⁶²⁶ Ex. 630, Vol. 27, Tab 35 (December 6, 1984, Memo from Dr. Naylor to File).

¹⁶²⁷ Ex. 743, Tab 37 (January 19, 1985, Plasma Production and Derivative Inventory Status Report).

¹⁶²⁸ Evidence of Mr. Jack Ryan, former President of Cutter, pp. 38774 - 38780.

¹⁶²⁹ Ex. 1001, Vol. 247, Tab 18 (February 26, 1985, Letter from Dr. Tom Walker to Dr. Wark Boucher).

date recommended by the Consensus Conference. On March 20, 1985, Dr. Naylor wrote to all CRCS Medical Directors advising that limited amounts of Factor IX would be delivered to the local blood centres for distribution during the transition period.¹⁶³⁰

852. One week later, the CRCS received information from Cutter that upset the plan. On March 27, 1985, a Cutter representative telephoned Dr. Tom Walker to advise that, as a result of "a potential delay of undetermined duration", heat-treated Factor IX would be delivered late. Estimated delivery dates were May 27, 1985 at the earliest or June 10, 1985 at the latest. Cutter cited ongoing delays with testing and release approvals by the OoB as the reason for the change in schedule. Although the BoB would accept heat-treated Factor IX samples pending finalization of labels, the OoB would not. Pursuant to U.S. regulations, the OoB would not release AHF for export nor commence the required quality, safety or efficacy assessments until labelling was finalized.¹⁶³¹

853. In response to Cutter's revised schedule, the CRCS took the following steps to help accelerate the label approval process:

- (a) Dr. Walker relayed to Cutter that its revised schedule was "unacceptable" and requested that Cutter attempt to reduce its label printing time by 6 - 8 weeks.¹⁶³²
- (b) Mr. Anhorn spoke with a senior Cutter official who promised to take every possible step to have the heat-treated Factor IX available by the May 1, 1985 deadline.¹⁶³³

¹⁶³⁰ Ex. 633, Vol. 30, Tab 7 (March 20, 1985, Memo from Dr. Naylor to CRCS Medical Directors).

¹⁶³¹ Ex. 1001, Vol. 247, Tab 47 (March 27, 1985, Memo from Dr. Tom Walker to Dr. Naylor re: Cutter Factor IX Labelling); and

Evidence of Dr. Davey, former Assistant National Director BTS, p. 30867-30871.

¹⁶³² Ex. 1001, Vol. 247, Tab 47 (March 27, 1985, Memo from Dr. Tom Walker to Dr. Naylor re: Cutter Factor IX Labelling).

¹⁶³³ Ibid.

- (c) Dr. Walker contacted the BoB to assist Cutter in obtaining necessary documentation including Cutter's license for heat-treated Factor IX and a letter from the BoB authorizing the list of factors to be included on the labels.¹⁶³⁴
- (d) Dr. Walker asked the BoB to intercede with the OoB to facilitate the labelling approval process.¹⁶³⁵

854. On April 13, 1985 Cutter was granted its heat-treated Factor IX license.¹⁶³⁶ However the license approved lots only for a 12 month period, which substantially reduced the shelf life of the heat-treated Factor. Obtaining approval for an extended shelf life required further approval by the BoB. This necessitated additional delay while the BoB reviewed Cutter's heat-treated Factor IX stability data.¹⁶³⁷

855. Despite the above concerns and potential delays, Cutter stated that it believed it could deliver all of the CRCS heat-treated Factor IX in time for the May 1, 1985 implementation date.¹⁶³⁸

856. The CRCS recognized that the status of Factor IX deliveries was uncertain despite Cutter's assurances. Accordingly, on April 29, 1985, Dr. Naylor wrote to all CRCS Medical Directors and advised that as of May 1, 1985, only limited amounts of heat-treated Factor IX

¹⁶³⁴ *Ibid*; and

Ex. 1002, Vol. 248, Tab 5 (April 9, 1985, Letter from Dr. Tom Walker to Dr. Wark Boucher re: Labelling for Heat-Treated Factor IX).

¹⁶³⁵ *Ex. 1001, Vol. 247, Tab 47 (March 27, 1985, Memo from Dr. Tom Walker to Dr. Naylor re: Cutter Factor IX Labelling).*

¹⁶³⁶ *Ex. 743, Tab 37 (November 1991, CRCS Table of Fractionation Product Licensing).*

¹⁶³⁷ *Ex. 934, Vol. 231, Tab 2 (April 18, 1985, Cutter Memo to File); and*

Ex. 743, Tab 37 (May 13, 1985, Memo from Dr. Tom Walker to Dr. Naylor re: Proposed Agenda for Cutter Meeting).

¹⁶³⁸ *Ex. 934, Vol. 231, Tab 2 (April 18, 1985, Cutter Memo to File).*

would be available. Specific requests were to be directed to the Blood Products Services division of the CRCS national office.¹⁶³⁹ This represented a change from Dr. Naylor's March 20, 1985 memo to Medical Directors in which he expected receipt of sufficient heat-treated Factor IX supplies to allow for distribution to all CRCS Blood Centres.¹⁶⁴⁰

857. The CRCS believed that it was prudent to maintain the limited heat-treated Factor IX inventory at its national office, because it anticipated that the limited amount available would be too small to decentralize among its 17 Blood Centres. Until supplies stabilized, maintaining the heat-treated Factor IX inventory at its national office would enable more efficient distribution in the event of an emergency. Requests for heat-treated Factor IX from hemophilia treaters, communicated through local Blood Centres, could be filled within a 24 hour period.¹⁶⁴¹

858. Notwithstanding Cutter's assurances, the May 1, 1985 delivery date was not met.

859. In order to address various problems associated with implementation of heat-treated concentrate, Dr. Naylor and Mr. Anhorn travelled to Cutter's North Carolina plant on May 15, 1985. The CRCS representatives were advised that heat-treated Factor IX labelling had been approved by the OoB, and that labelling and packaging of its first lot prepared from CRCS plasma would proceed as soon as possible.¹⁶⁴²

860. Canadian regulatory approval was not confirmed until May 31, 1985, when Dr. Liston, Assistant Deputy Minister of Health, provided Cutter with its Notice of Compliance for heat-treated Factor IX Complex.¹⁶⁴³

¹⁶³⁹ Ex. 634, Vol. 31, Tab 29 (April 19, 1985, Memo from Dr. Naylor to CRCS Medical Directors).

¹⁶⁴⁰ Ex. 633, Vol. 30, Tab 7 (March 20, 1985, Memo from Dr. Naylor to CRCS Medical Directors).

¹⁶⁴¹ Ex. 635, Vol. 32, Tab 36 (May 30, 1985, Memo from Dr. Naylor to CRCS Medical Directors); and

Evidence of Dr. Davey, former Assistant National Director BTS, pp. 30872 - 30874.

¹⁶⁴² Ex. 934, Vol. 231, Tab 9, p. 4 (May 15, 1985, Dr. Naylor Trip Report to Cutter, North Carolina).

¹⁶⁴³ Ex. 934, Vol. 231, Tab 12 (May 31, 1985, Letter from Dr. Liston to Cutter).

861. Cutter's first shipment of heat-treated Factor IX (Lot C9P001 - 3,753 vials) was delivered to the CRCS on May 30, 1985.¹⁶⁴⁴ That same day, Dr. Naylor wrote to all CRCS Medical Directors advising *inter alia* that limited supplies were available by request, but that supplies were expected to stabilize by mid-August.¹⁶⁴⁵ Subsequent deliveries were not received until July 8, 1985 (Lot C9N005A - 3,824 vials and Lot C9N006A - 5,539 vials).

862. Thus, despite the efforts of the CRCS to help expedite the approval and release of Cutter's heat-treated Factor IX, a myriad of overlapping regulations delayed the introduction of heat-treated Factor IX in Canada until May 30, 1985. The first delivery was made approximately six months after the first lot of CRCS plasma had been heat-treated in vial, and approximately two months later than Cutter's originally estimated release date.¹⁶⁴⁶

6) "Depletion" and "Write-Off" of Non-heat-treated Inventory

a) "Depletion"

863. It has been alleged that the CRCS did not want to begin distributing heat-treated concentrate until it had depleted its non-heat-treated inventory and that it misled others about the availability of heat-treated concentrate. It was suggested by various counsel¹⁶⁴⁷ that the CRCS geared its implementation schedule to estimated dates of depletion of its heat-treated inventory

¹⁶⁴⁴ Ex. 638, Vol. 35, Tab 39 (Table 7, September 27, 1985 Craig Anhorn Position Paper re: Implementation of Heat-Treated Factor VIII and IX Distribution).

¹⁶⁴⁵ Ex. 635, Vol. 32, Tab 36 (May 30, 1985, Memo from Dr. Naylor to CRCS Medical Directors).

¹⁶⁴⁶ Ex. 638, Vol. 35, Tab 39 (Table 7, September 27, 1985 Craig Anhorn Position Paper re: Implementation of Heat-Treated Factor VIII and IX Distribution); and

Ex. 743, Tab 37 (Attachment #10 (CRCS Stock Record Card for Cutter Heat-Treated Factor IX Lots C9P001 and C9N005A).

¹⁶⁴⁷ See for example: Cross-Examination by Ms. B. Tough at p. 29436; and

Cross Examination by Mr. D. Doucette at p. 39343-39346.

instead of dates when heat-treated concentrate became available. This allegation is false. It was completely denied in *viva voce* evidence of the CRCS. The accusation relies primarily upon misinterpretations of written statements that are ambiguous and taken out of context.

864. Some counsel have suggested that the following text from Dr. Naylor's Consensus Conference presentation indicates that the CRCS intended to use up its inventory of non-heat-treated product:¹⁶⁴⁸

Although [implementation of heat-treated concentrate] cannot be done overnight, we estimate that it will be possible to do this within a period of 8 weeks once all untreated products have been utilized and at the time the first deliveries are made of heat-treated concentrates.

...

Current total inventories of untreated concentrate at BTS Centres, National warehouse and in process at Cutter and Connaught amounts to 18,230,400 units. At average rates of distribution, this is just over 22 weeks supply, as of December 1st, 1984 and thus these [supplies] will be exhausted by about May 1st, 1985. By this time, the CRCS BTS should also have received the first shipments of heat-treated Factor VIII concentrate prepared from CRC plasma and the first deliveries of the supplementary commercial purchase of similar product.

To ensure a complete conversion to heat-treated Factor VIII within a period of 8 weeks following the May 1st introduction date, it may be necessary to move inventories of unheated product from regions where there may be excess to others in short supply, to ensure that supplies of untreated product are exhausted across the country at more or less the same time.¹⁶⁴⁹

865. According to Dr. Davey who attended the conference:

DR. DAVEY: Well, I think it is evident that Dr. Naylor's concept was that heat-treated products should be offered on a uniform basis across Canada, and if there were a period of restricted supply - that should be across the country. So that when necessary, the stock of all product would be redistributed to allow the general distribution. But there would not be any area in which only treated

¹⁶⁴⁸ *Cross-Examination by Mr. Doucette pp. 39259-39261; and*

Cross-Examination by Ms. Edwardh, pp. 35713-35714.

¹⁶⁴⁹ *Ex. 631, Vol. 28, Tab 1, pp. 2, 4-5 (December 10, 1984, Dr. Naylor Presentation).*

product was distributed, nor any area in which only heat-treated product was distributed. This is a national - I have emphasized before this was a plan for national introduction, complete replacement and with no hiatus in supply either before, if possible, either before or after the complete replacement.¹⁶⁵⁰

866. Mr. Fred Anderson, a representative of the CBC who attended this conference, had no recollection of any discussion concerning the forced depletion of untreated product. He stated that the above point concerned the scheduling of the introduction of heat-treated product if there were inadequate supplies of heat-treated product available. Regardless of any discussions that may have taken place within the context of the conference, at no time did he believe the implementation of heat-treated product was to be based on the utilization or depletion of non-heat-treated material:

I think I came away at the time thinking that it was going to have to be inventory written off at the end.¹⁶⁵¹

867. Dr. Inwood testified that, as a result of the discussions at the Consensus Conference, he was under the impression that the CRCS intended to deplete its non-heat-treated inventory.¹⁶⁵² However, Dr. Inwood's evidence on this point was confused and inconsistent, and could be interpreted as being equally consistent with the CRCS position that full conversion to heat-treated concentrate would occur as soon as sufficient supply was available. Commission counsel attempted to extract an admission from Dr. Inwood that Dr. Naylor did not want to distribute heat-treated concentrate until *after* all heat-treated inventory was depleted. In response, Dr. Inwood stated his opinion that the CRCS wanted to "finish off" its non-heat-treated inventory *at the same time* it began distributing heat-treated concentrate. This, of course, was entirely consistent with the CRCS position and the position adopted by the Consensus Conference that acknowledged the need to distribute both forms of concentrate during the transition period. Furthermore, Dr. Inwood acknowledged that Dr. Naylor's comments meant

¹⁶⁵⁰ Evidence of Dr. Davey, former assistant National Director BTS, pp. 30840-30841.

¹⁶⁵¹ Evidence of Mr. Fred Anderson, CBC Representative, pp. 35714-35719

¹⁶⁵² Evidence of Dr. Inwood, Hemophilia Treater, pp. 33476 - 33477.

that the CRCS had no alternative but to continue distributing non-heat-treated concentrate until sufficient quantities of heat-treated concentrate were received:

DR. INWOOD: To do justice to the late Dr. Naylor, I suspect that what he wants to get across to us is his opinion that they would not be able to get any heat-treated material until April, and as a result, we would have to continue using non-heat-treated material ... the implication was they could not get any material before April, and therefore, as a consequence, it just so happens, parenthetically, that the non-heat-treated materials would have to be used up.¹⁶⁵³

868. The argument that the CRCS had the intention of depleting all of its non-heat-treated product is inconsistent and ignores attempts of the CRCS to obtain information and product from Cutter, Hyland and Armour regarding the availability of heat-treated concentrate.

¹⁶⁵³ *Evidence of Dr. Inwood, Hemophilia Treater, p. 33476.*

excess fractionation capacity and licensing. Furthermore, it disregards the evidence of the fractionators confirming the short supply of heat-treated concentrate.¹⁶⁵⁴

869. Based on supply information obtained from fractionators, the CRCS recognized that implementation could not occur without a transition period during which both heat-treated and non-heat-treated concentrates would be distributed. This aspect of the plan was not controversial and the proposition was accepted by the participants at the Consensus Conference and subsequently by the CBC Executive Committee.¹⁶⁵⁵

¹⁶⁵⁴ Ex. 630, Vol. 27, Tab 25 (November 26, 1984, Memo from Craig Anhorn to File re: Cutter Heat-Treated Factor VIII and IX);

Ex. 630, Vol. 27, Tab 28 (November 26, 1984, Telex from Dr. Naylor to Alpha Therapeutics, Armour, Cutter and Fenwal);

Ex. 630, Vol. 27, Tab 31 (November 29, 1984, Memo from Dr. Naylor to File re: CBC Consensus Meeting Conversations with Canadian Fractionators);

Ex. 630, Vol. 27, Tab 35 (December 6, 1984, Memo from Dr. Naylor to File re: Heat-Treated Coagulation Factor Products - The Meeting Held on December 4, 1984 with Cutter Laboratories Representatives);

Ex. 630, Vol. 27, Tab 37 (December 6, 1984, Memo from Dr. Naylor to File re: Meeting with Travenol Representatives to Discuss Hyland Heat-Treated Coagulation Factor Products);

Ex. 630, Vol. 27, Tab 38 (December 6, 1984, Memo from Dr. Naylor to File re: Meeting with Armour Pharmaceutical Representatives to Discuss Heat-Treated Coagulation Factor Products);

Ex. 632, Vol. 29, Tab 27 (February 18, 1985, Letter from Dr. Davey to Dr. Leclerc-Chevalier re: 1985 Supplementary Purchase of Factor VIII);

Evidence of Mr. Larry Alderson, Product Specialist, Hyland/Baxter/Fenwal, pp. 38986 - 38988;

Evidence of Jack Ryan, Former President, Cutter Laboratories, pp. 38741 - 38742; 38748-38750; 38752-38753; and

Ex. 935, Vol. 234, Tab 52 (Cutter Finished Goods Inventory U.S. Commercial Report).

¹⁶⁵⁵ Ex. 631, Vol. 28, Tab 1 (Recommendations of the Consensus Conference on Heat-Treated Factor VIII, December 10, 1984).

870. In his presentation at the Consensus Conference, Dr. Card made it clear that a "conversion period" was expected, although he hoped it would not exceed one to three months.¹⁶⁵⁶ He spoke of the need for criteria to determine which patients received heat-treated concentrate during the transition. He recognized the practical necessity for, and expressed no objection to, distributing non-heat-treated concentrate to the majority of hemophiliacs who did not satisfy the appropriate criteria. He saw no reason to provide preferential treatment to patients who had received multiple infusions of non-heat-treated concentrate. As he candidly pointed out during his speech at the conference, it was likely that these patients had already been exposed to the AIDS virus and were probably immune. For this reason, it was logical to reserve the heat-treated concentrate during the conversion period for low risk patients who had received very little or no factor concentrates:

There is an important point which must be made at this time and it relates to the ultimate implementation strategy. For the severe hemophiliac who has received multiple infusions in the past three years (say 40,000 units per year), it is likely that he has been exposed and even likely that immunity has developed. However, even if a product were available today that absolutely removed the AIDS risk, the unfortunate patients who are destined to develop AIDS in the next two years are almost certainly in their incubation period. Nothing we will do today will change that. Indeed, no matter what we do today it is almost certain that there will be an increase in AIDS cases in hemophiliacs over the next year. This should be very clear and understood by both the treaters and the patients.

...

For the severe hemophiliac, on multiple doses of concentrate, I believe, as stated above, that introduction of heat-treated product will have little effect upon immediate risk of AIDS and ultimate outcome. I would therefore propose that factor VIII be issued either as heat-treated or non-heat-treated as it becomes available depending on the logistics until all non-heat-treated is gone. I would not propose any preferential consideration in this group.

...

However, for the hemophiliac who has not been exposed to factor VIII concentrates previously the risk of receiving non-heat-treated concentrates is likely very high ... For this group any need for concentrate during [the

¹⁶⁵⁶ Ex. 631, Vol. 28, Tab 1, pp. 4-5 (December 10, 1984, Presentation of Dr. Card).

conversion period] should be considered a mandatory consideration for receiving heat-treated product.¹⁶⁵⁷ (Emphasis original)

871. In his conclusion, Dr. Card re-emphasized the rationale for a priority list and the need for non-heat-treated concentrate during the conversion period:

We propose an implementation strategy that sees heat-treated factor introduced as available, without any geographic preference, and in essence sees the severe multiply-treated hemophiliacs using up the stocks of non-heat-treated product. Essential to our proposal is that in the rare situation whereby a newly diagnosed or mild hemophiliac requires concentrate in the conversion period that a mechanism be established to direct heat-treated concentrate to that patient. Monitoring would be by the Hemophiliac Clinic Directors".¹⁶⁵⁸

Dr. Card's concept of rationing heat-treated concentrate echoed Mr. Mindell's recommendation for a "scheduled hierarchy of utilization" during an estimated six-month period "until all concentrate distributed in Canada meet BoB standards".¹⁶⁵⁹ This priority list was further developed by the Ontario CHS MSAC and subsequently approved and utilized by the National CHS MSAC and National CHS Board.¹⁶⁶⁰

872. CRCS statements about "depletion" or "exhaustion" of non-heat-treated inventory can only be understood when interpreted in conjunction with the supply information it received from the fractionators and the rationale and need for a prioritized distribution of heat-treated concentrate. It was imperative to have an adequate supply of product in the implementation

¹⁶⁵⁷ Ex. 631, Vol. 28, Tab 1, pp. 2-3, 5 (December 10, 1984, Presentation of Dr. Card).

¹⁶⁵⁸ Ex. 631, Vol. 28, Tab 1, p. 6 (December 10, 1984, Presentation of Dr. Card) but note his testimony at p. 31730-31740 wherein he modified his position.

¹⁶⁵⁹ Ex. 630, Vol. 27, Tab 44, p. 6 (December 8, 1984, Memo from William Mindell to Ontario and National CHS and MSACs).

¹⁶⁶⁰ Ex. 634, Vol. 31, Tab 20 (April 19, 1985, Minutes of CHS MSAC); and

Ex. 634, Vol. 31, Tab 26 (April 25, 1985, Letter from Dr. Card to Dr. Naylor re: Heat-Treated Factors Concentrates and Implementation Period).

period. As Dr. Card pointed out, the majority of hemophiliacs had already received multiple infusions of non-heat-treated concentrate and would not be eligible to receive heat-treated concentrate during the transition period. Nevertheless, they would continue to require factor therapy throughout the transition period. The CRCS, the CHS and treaters were well aware that failing to supply concentrate when it was required could expose hemophiliacs to potentially life threatening bleeds. By necessity, the CRCS had to be concerned if and when its non-heat-treated inventory might be depleted in order to plan for and maintain an adequate supply of concentrate to treat these patients. To ignore this reality would have been irresponsible and a violation of the Consensus Conference recommendations.

b) "Write-Off"

873. The CRCS had no motive to deplete its non-heat-treated inventory prior to the general implementation of heat-treated concentrate on July 1, 1985. It did not stand to gain by using up non-heat-treated inventory nor did it stand to lose by converting to heat-treated concentrate while non-heat-treated concentrate remained in its inventory. CRCS did not intentionally set out to deplete its non-heat-treated inventory because it feared being held financially responsible for "writing-off" unused non-heat-treated concentrate. Proponents of this theory allege that, in order to avoid a stiff financial penalty, the CRCS national office and selected Medical Directors intentionally distributed as much non heat treated concentrate as possible to hospitals and clinics. Such a theory is false. It is primarily based upon misinterpretations of written statements that are vague and taken out of context. It was denied by every witness who was asked about it, from the CRCS and the CBC. Comments contained in the minutes of a December 11, 1984 CBC Executive Committee meeting and a June 20, 1985 memo from Mr. Anhorn to Dr. Naylor are cited in support of such allegations. The significance of these documents is discussed below.

874. On December 11, 1984, the CBC Executive Committee met and endorsed the Consensus Conference recommendations. The minutes record that during a discussion of the implementation of heat-treated concentrate, Dr. Perrault raised the write-off issue:

Dr. Perrault added that, as far as he is concerned, the inventory has to be dealt with, unless the CBC tells him to write it off, which was not requested by the Conference and more specifically by the Canadian Hemophilia Society.¹⁶⁶¹

It has been alleged that this statement indicates that the CRCS was so concerned about its potential financial exposure for left over non-heat-treated concentrate that it specifically requested permission to have it written off. It has been further alleged that, in absence of such permission, the inventory would be "dealt with" or, in other words, "depleted" by the CRCS.

875. Dr. Perrault was not questioned about this particular minute. Ambrose Hearn, who chaired the CBC Executive Committee meeting, testified that he had no idea what this ambiguously worded statement meant.¹⁶⁶² Fred Anderson, who was also a member of the CBC Executive Committee, agreed, noting that the minute did not explain how Dr. Perrault proposed to deal with the inventory. Despite the imprecise language of the written comment, Mr. Anderson was confident that Dr. Perrault's position at that meeting was consistent with the role of the CRCS to implement heat-treated concentrate as soon as possible:

PERRAULT: He doesn't say in which way he is going to deal with the inventory. He simply says he is going to deal with the inventory. I think he understands fully, completely that the Red Cross's role is to introduce this program as quickly as is possible ...

In fact, as you know, he chaired the Consensus Conference. So for him not to understand the sense of tone of that recommendation is beyond what I could comprehend ...¹⁶⁶³

876. Whatever the meaning of the phrase "the inventory has to be dealt with", it is illogical to conclude from this minute that Dr. Perrault was worried that the CRCS would be

¹⁶⁶¹ Ex. 860, Vol. 192, Tab 4, p. 8544, para. 28 (December 11, 1984, Minutes of CBC Executive Committee).

¹⁶⁶² Evidence of Ambrose Hearn, former Chair of CBC, pp. 35774 - 35778.

¹⁶⁶³ Evidence of Fred Anderson, Member of CBC Executive Committee, pp. 35775 - 35776.

held financially responsible for the withdrawal of non-heat-treated concentrate. Because the conversion to heat-treated concentrate was specifically ordered by the BoB, any costs associated with the conversion would be borne by the CBC as legitimate blood program expenses. ~ This is entirely consistent with the CBC's acknowledgment that it was prepared to authorize the implementation of heat-treated concentrate regardless of the cost. It is noteworthy that just prior to Dr. Perrault's statement regarding the inventory, the minutes record the CBC's willingness to fully fund the conversion:

For the Chairman, the issue is two-fold: first, there is a need for developing information on all costs associated with heat-treated Factor VIII and necessary arrangements could be made for this purpose between the CBC Secretariat and the Red Cross; secondly, decisions have to be taken on the recommendations regardless of cost development.¹⁶⁶⁵

877. Craig Anhorn's June 20, 1985 memo to Dr. Naylor regarding the cost implications of the withdrawal of non-heat-treated concentrate has also been cited in support of the planned depletion theory. In the first paragraph of the memo, Mr. Anhorn projected a write-off of approximately \$250,000.00 for non-heat-treated Factor VIII and Factor IX remaining in CRCS inventory on July 1, 1985. Commenting specifically on Factor VIII, he wrote:

based on previous projections of inventories of this product going to zero by June 17th, and the knowledge that not all Centres have co-operated fully in the final distribution of this product it is estimated that the final inventory in CRC hands will be approximately 500,000 AHF units.¹⁶⁶⁶

878. In the balance of the memo, Mr. Anhorn discussed the issue of how to deal with returns of non-heat-treated concentrate from hospitals and whether the provinces should be credited for the returns. Mr. Anhorn listed three options, one of which was not to credit the

¹⁶⁶⁴ *Evidence of Dr. Perrault, former National Director BTS, pp. 29447, 29923 - 29934, 30847.*

¹⁶⁶⁵ *Ex. 860, Vol. 192, Tab 4, p. 8544, para. 26 (December 11, 1984, Minutes of the CBC Executive Committee Meeting).*

¹⁶⁶⁶ *Ex. 877, Vol. 209, Tab 5, p. 1234, para. 1(a) (June 20, 1985, Memo from Craig Anhorn to Dr. Naylor).*

provinces for the returns; however, Mr. Anhorn noted that this option could leave the CRCS open to criticism:

Option b) while the best for CRC cash position would place the CRC in a position whereby the provinces could imply we had dumped product in the hospitals to cut losses.¹⁶⁶⁷

Mr. Anhorn concluded the memo with a recommendation that the provinces be credited for a portion of returns (50% of the total amount supplied in June 1985 to each province), which would limit financial liability to the provinces:

This assumes a two week supply in the field and limits the CRC liability to the provinces to approximately 2,000,000 units or approximately \$210,000.¹⁶⁶⁸

879. It has been suggested that the above passages demonstrate a plan to "dump" non-heat-treated concentrate into hospital inventories in order to limit CRCS financial "liability" to the provinces. This allegation is inconsistent with and wholly unsupported by a considerable body of documentary evidence and testimony given by numerous witnesses as discussed below.

880. Mr. Anhorn dismissed the suggestion that the CRCS used the eight week transition period as an opportunity to "run down" its inventory of non-heat-treated concentrate.¹⁶⁶⁹ He testified to the contrary, noting that the financial aspect of the proposed write-off was primarily an administrative housekeeping matter and was of no real concern to the CRCS.¹⁶⁷⁰ This was reflected in paragraph 2 of his June 20, 1985 memo wherein he characterized the write-off of non-heat-treated concentrate in CRCS inventories as a "given":

¹⁶⁶⁷ *Ibid*, p. 1235, para. 6.

¹⁶⁶⁸ *Ibid*, p. 1235, para. 8.

¹⁶⁶⁹ *Evidence of Craig Anhorn, former Blood Product Manager, CRC BTS*, p. 39343.

¹⁶⁷⁰ *Evidence of Craig Anhorn, former Blood Product Manager CRC BTS*, p. 39344.

As we have previously discussed, this write-off was a "given" when the decision was made to introduce the heat treated product in December 1984. The question now is "should the CRC credit the hospitals for all product returned".¹⁶⁷¹

Mr. Anhorn testified that the write-off of CRCS and hospital inventories was significant only insofar as it was necessary to determine how it could be handled from an accounting or bookkeeping point of view.¹⁶⁷²

881. Mr. Anhorn testified that it was always understood that the CBC would bear the costs of the write-off and replacement of non-heat-treated concentrate. At the December 10, 1984 Consensus Conference, Mr. Anderson, of the CBC, assured Mr. Anhorn that cost was not a concern:

ANHORN: Mr. Anderson, when I asked the question on cost, said "Don't worry about it Craig, this is not about cost, this is about getting it done quickly".¹⁶⁷³

This assurance was also reflected in the December 11, 1984 minutes of the CBC Executive Committee meeting as discussed above.¹⁶⁷⁴

882. While the language of Mr. Anhorn's June 20, 1985 memo did not clearly distinguish between CRCS and blood program accounting measures, there was never any doubt that all costs associated with the write-off and replacement were ultimately the responsibility of the CBC. Mr. Anhorn, the CRCS and the CBC knew that these expenses would be charged to

¹⁶⁷¹ Ex. 877, Vol. 209, Tab 5, p. 1234, para. 2 (June 20, 1985, Memo from Craig Anhorn to Dr. Naylor).

¹⁶⁷² Evidence of Craig Anhorn, former Blood Products Manager, CRC BTS, pp. 39505 - 39506.

¹⁶⁷³ Evidence of Craig Anhorn, former Blood Products Manager, CRC BTS, pp. 39503 - 39505.

¹⁶⁷⁴ Ex. 860, Vol. 192, Tab 4, p. 8544, para. 26 (December 11, 1984, Minutes of the CBC Executive Committee Meeting).

the blood program fractionation account which the CRCS held in trust for the CBC.¹⁶⁷⁵ At no time did the CRCS consider that it might have to pay for these blood program expenses out of its own funds.¹⁶⁷⁶

883. This view was reflected in the testimony of CBC members Messrs. Anderson, Hearn and Glynn.¹⁶⁷⁷ Stephen Dreezer's comments on the write-off issue were succinct:

DREEZER: It was written off. From a purely financial point of view, the impact on the Red Cross was zero ... because writing that off would have been done using [CBC] funds from the fractionation account.¹⁶⁷⁸

884. Randall Klotz and Elaine Boily of the CBC Secretariat also testified that the CBC *not* the CRCS would be financially accountable for the write-off and withdrawal of non-heat-treated concentrate. Randall Klotz testified:

KLOTZ: ... I don't recall at any time the CBC behaving or suggesting that the Red Cross would be left vulnerable for a blood product or a plasma fraction that had been acquired or developed or prepared for distribution in good faith in this system.

I think we were focusing more, looking at the issue of how would we deal with it financially or mechanically ...

And there may be cash flow consequences, but I don't think there was ever a question on the ultimate accountability and the linkage of that product to the funder.¹⁶⁷⁹

¹⁶⁷⁵ Evidence of Claude Morin, former National Administrator, CRC BTS, pp. 39832-39834; 39935; and 40027-40036.

¹⁶⁷⁶ Evidence of Craig Anhorn, former Blood Products Manager, CRC BTS, pp. 39505-39506.

¹⁶⁷⁷ Evidence of Mr. Dreezer, Mr. Anderson, Mr. Hearn and Mr. Glynn, CBC Panel, pp. 35780-35783; and 36125-36129.

¹⁶⁷⁸ Evidence of Stephen Dreezer, CBC Panel, pp. 35743-35745.

¹⁶⁷⁹ Evidence of Randall Klotz, former Member of the CBC Secretariat, pp. 36895-36896.

Mr. Klotz' testimony is consistent with the July 22, 1985 letter he wrote to Dr. Davey regarding the return of non-heat-treated concentrate. This letter confirmed that the issue regarding hospital returns was not whether but how to account for concentrate that had been billed to the provinces. Nowhere in the letter did Mr. Klotz suggest that the CRCS would be financially liable for the cost of returned concentrate.¹⁶⁸⁰

885. The text of the October 17, 1985 memo written by Ms. Wildgoose, a CRC BTS administrator, documenting a telephone conversation she had with Mr. Klotz regarding provincial credits for returned concentrates emphasizes that the write-off issue was primarily an accounting matter for which the CBC was responsible. It is clear from this document that the credit was included in invoices to Québec and applied against the fractionation account. The details and logistics of this cashless transaction confirmed that credits to other provinces, had they been issued, would have been applied against CBC funds held in the fractionation account.¹⁶⁸¹

886. A position paper prepared for the December 16-17, 1985 CBC meeting and the subsequent minutes of that meeting reads as follows:

Whether the returns are written off or refunded to provinces, the provinces will end up paying for both productions out of the Fractionation Account...

The cost of unusable non-heat-treated Factors VIII and IX is a Blood Programme cost and hence a funding responsibility of the CBC funding governments (barring negligence or mismanagement at the Society).¹⁶⁸²

¹⁶⁸⁰ Ex. 877, Vol. 209, Tab 24 (July 22, 1985 Letter from Randall Klotz to Dr. Davey).

¹⁶⁸¹ Ex. 692 (October 17, 1985 Memo by Betty Wildgoose re. Telephone Conversation with Randall Klotz).

¹⁶⁸² Ex. 862, Vol. 194, Tab 2, p. 53, paras. 2 and 3 (CBC Secretariat Position Paper for December 16 - 17, 1985 CBC Meeting).

In his testimony, Mr. Klotz confirmed that there was never any issue of negligence or mismanagement on the part of the CRCS regarding the transition to heat treated concentrate or the write-off and withdrawal of non-heat-treated concentrate.¹⁶⁸³

887. Elaine Boily explained why there was no specific statement contained in the CBC minutes authorizing the CRCS to write-off the non-heat-treated concentrate:

Although I don't have an express recollection of something being expressly stated in that fashion, my general recollection and impression at that time was that it was a given. The BoB had issued a directive for ... non-heat-treated coagulation factor products to be switched over to heat-treated as soon as possible, from the Red Cross point of view and as soon as feasible from the manufacturer's point of view.

And my feeling was, at that time ... this was a blood program related cost and the CBC was going to cover whatever was inherent in that decision. And that could very well be why it is not minuted anywhere.¹⁶⁸⁴

Ms. Boily's testimony is logical considering the CRCS did not require the CBC's permission to write-off factor concentrate in its inventory. The write-off of factor concentrate was not unprecedented. For example, in 1984, the CRCS wrote off \$90,000 worth of concentrate against the fractionation account.¹⁶⁸⁵

888. The documents and testimony referred to above demonstrate that members of the CRCS and the CBC clearly understood that the CRCS would not have to pay for the write-off and withdrawal of non-heat-treated concentrate. Given the knowledge that the CBC would ultimately be responsible for these legitimate blood program costs, the CRCS had no reason or motive to intentionally deplete its inventory of non-heat-treated concentrate.

¹⁶⁸³ Evidence of Mr. Klotz, former Member of the CBC Secretariat, pp. 37001-37004.

¹⁶⁸⁴ Evidence of Elaine Boily, former Member of the CBC Secretariat, pp. 36897 - 36898.

¹⁶⁸⁵ Ex. 958, Vol. 289, Tab 3 (April 5, 1985 CRCS General Ledger Trial Balance for Month Ending December 31, 1984).

7) Transition to Enhanced Virally Inactivated Factor Concentrate

889. Following the transition to heat-treated concentrate in 1985, the CRCS continued to monitor the development of technological advances in the heat-treatment process. "wet heat-treated", "vapour" or "steam treated" AHF were among the second generation of enhanced virally-inactivated factor concentrates being developed by various fractionators to improve upon the conventional "dry" heat-treatment process. Recognizing the potential for improved safety, the CRCS acted promptly to secure a sufficient supply of this new, state-of-the-art concentrate for Canadian hemophiliacs. The CRCS was one of the first blood suppliers in the world to fully convert to enhanced virally inactivated AHF, and, as a result, it managed to avoid the impact of world-wide shortages as demand for this technologically advanced concentrate increased.¹⁶⁸⁶

890. Details of events precipitating this conversion and those describing CRCS efforts to execute implementation are set out below.

a) **Problems With Armour's Dry Heat-Treated Factor Concentrate**

891. At the time of conversion to heat-treated concentrate in 1985, Armour, like other North American fractionators, utilized a "dry" heat-treatment process. However, no two fractionators' processes were exactly the same. Each utilized a slightly different technique to inactivate viruses.¹⁶⁸⁷ Armour's process differed from Cutter's in that it did not incorporate protein stabilizers. Without these stabilizers, which had a tendency to protect viruses from heat, Armour's process claimed to inactivate more virus with less heat in less time. For example, Cutter's process required heating at 68°C for 72 hours while Armour's required heating at 60°C for only 30 hours. By comparison, Alpha's dry heat-treatment process, which was not licensed

¹⁶⁸⁶ Ex. 772, Vol. 178, Tab 46 (April 18, 1986, Memo from Bill Mindell, Chair CHS Blood Resources Committee to Elaine Woloschuk and Bob Shearer re: Nomination of Stephen Vick and Dr. Brian McSheffery for Special Appreciation Awards at 1989 Annual Meeting).

¹⁶⁸⁷ Evidence of Dr. Davey, former Assistant National Director BTS, pp. 26984 - 26985.

in Canada, required even less time at 60°C for 20 hours.¹⁶⁸⁸ As a precondition to its licensure in Canada, Armour provided data to the BoB supporting the ability of Armour's process to inactivate the AIDS virus. The BoB was sufficiently impressed by this data and granted Armour its license on April 12, 1985.¹⁶⁸⁹

892. Initial concerns about the effectiveness of the dry heat-treatment process were focused primarily on hepatitis not HIV transmission. Attendees at a November 1985 joint NHF/CHS conference in Houston, Texas, discussed evidence that wet heat-treated or steam treated Factor VIII concentrates reduced the risk of hepatitis transmission. The CRCS was very interested in this new process and, in response to a request from several CHS MSAC members who attended the conference, Dr. Naylor recommended that the CRCS participate in a pilot study to assess the effectiveness of wet heat-treated Factor VIII concentrate among newly-diagnosed hemophiliacs.¹⁶⁹⁰ This project was subsequently organized by the WHF, CDC and NHF with Canadian participation co-ordinated by hemophilia treaters, Drs. Inwood and Rivard. The CRCS lent its support to this project and arranged for the purchase of a limited amount of Immuno's vapour treated Factor VIII concentrate for distribution with the appropriate approval from the BoB.¹⁶⁹¹

893. In June 1986, questions were raised for the first time about the effectiveness of Armour's heat-treatment process in inactivating the AIDS virus. On Friday, June 27, 1986, Armour wrote to the CRCS about three U.S. cases of HIV seroconversions possibly associated with Armour's heat-treated Factor VIII. All three hemophiliacs had been infused with heat-treated concentrate produced from plasma collected prior to anti-HIV testing in 1985. Armour

¹⁶⁸⁸ *Evidence of Dr. Davey, former Assistant National Director BTS, pp. 26949 - 26952.*

¹⁶⁸⁹ *Ex. 743, Tab 37 (November 1991 CRCS Table: Fractionation Product Licensing); and*

Evidence of Dr. Davey, former Assistant National Director BTS, pp. 26984.

¹⁶⁹⁰ *Ex. 641, Vol. 38, Tab 3 (November 27, 1985, Memo from Dr. Naylor to Dr. Davey re: Heat-Treated Factor VIII Concentrate for Use in Newly-Diagnosed Hemophilia A Patients).*

¹⁶⁹¹ *Ex. 766, Vol. 172, Tab 51 (July 4, 1986, Letter from Mr. Craig Anhorn to Dr. Wark Boucher, BoB re: Immuno Vapour Treated Factor VIII Concentrate).*

was careful to point out that circumstances surrounding each case prevented a definitive conclusion regarding the cause of the seroconversions. Nevertheless, Armour decided to withdraw all lots of heat-treated Factor VIII produced from non-HIV screened plasma.¹⁶⁹²

894. In response, Dr. Davey wrote to all Medical Directors on Monday, June 30, 1986 and instructed them to withdraw all lots of Armour's untested heat-treated Factor VIII. The memo included a list of withdrawn lot numbers, and a copy of Armour's letter explaining the rationale for the voluntary withdrawal. In order to keep others informed of this development, Dr. Davey copied this memo to hemophiliac representatives Dr. Card, Chair of the CHS MSAC, and Ed Gurney, Executive Director of the CHS.¹⁶⁹³

895. The CRCS continued to press Armour for further details regarding its voluntary withdrawal. On July 31, 1986, Dr. Davey, on behalf of Dr. Card and the CHS MSAC, wrote to Armour requesting more information about the efficacy of Armour's heat-treatment process.¹⁶⁹⁴ Meanwhile, the CRCS continued to monitor and record the withdrawal of untested heat-treated Armour AHF in Canada.¹⁶⁹⁵ By October, 1986, the CRCS reported to the BoB that approximately 480,000 units of untested heat-treated Armour Factor VIII had been returned.¹⁶⁹⁶

¹⁶⁹² Ex. 766, Vol. 172, Tab 46 (June 27, 1986, Letter from Rorer Canada Inc. (Armour) to Dr. Davey).

¹⁶⁹³ Ex. 766, Vol. 172, Tab 47 (June 30, 1986, Memo from Dr. Davey to CRCS Medical Directors re: Withdrawal of Armour Factor VIII Concentrate).

¹⁶⁹⁴ Ex. 766, Vol. 172, Tab 60 (July 31, 1986, Letter from Dr. Davey to Dr. Card re: Armour withdrawal of Factor VIII); and

Ex. 766, Vol. 172, Tab 61 (July 31, 1986, Letter from Dr. Davey to Armour re: withdrawal of Factor VIII).

¹⁶⁹⁵ Ex. 646, Vol. 43, Tab 22 (September 10, 1986, Memo from Joanne Wilson, Acting Manager (Operations) BPS to Mr. Steven Vick, Deputy Director BPS re: updated summary of Armour Factor VIII withdrawal).

¹⁶⁹⁶ Ex. 767, Vol. 173, Tab 13 (October 8, 1986, Letter from Mr. Steven Vick to Dr. Wark Boucher, BoB re: Armour Factor VIII).

896. Further concerns about Armour's heat-treatment process were raised on October 7, 1986, when the CRCS received a telex indicating that all Armour heat-treated Factor VIII (tested and untested) was being withdrawn from Britain. This action was taken after the British government received the reports of two patients developing AIDS and associated with their use of Armour's untested heat-treated Factor VIII. Following the receipt of Armour's telex, the CRCS consulted representatives from the BoB, the CBC and the CHS MSAC on an almost daily basis. Numerous discussions were held in an effort to determine whether a similar expanded Armour withdrawal was warranted in Canada.

Details concerning CRCS efforts in this regard are set below:

- (a) Immediately after receiving the Armour press release, the CRCS took the following steps:¹⁶⁹⁷
 - (i) Dr. Tom Walker and Mr. Vick met with Dr. Perrault and thereafter contacted the BoB for guidance on whether or not to implement an expanded Armour withdrawal.
 - (ii) All distribution of Armour factor concentrate from CRCS national office was suspended pending a final decision on an expanded Armour withdrawal.
- (b) On October 8, 1986, the CRCS took the following steps:¹⁶⁹⁸
 - (i) Mr. Vick contacted both Cutter and the American Red Cross requesting information about the availability of replacement heat-treated product. Cutter reported that it could set aside 10 million units of heat-treated AHF until October 10, 1986, while the AmCross could provide up to 5 million units, if necessary,

¹⁶⁹⁷ Ex. 660A, Vol. 58, Tab 25 (October 8 - 17, 1986, Handwritten Notes of Steven Vick and Dr. Tom Walker re: Discussions of Armour Withdrawal).

¹⁶⁹⁸ *Ibid.*

for delivery by late December 1986. After reviewing the amount of untested heat-treated Armour AHF in distribution, Mr. Vick determined that replacement purchases from Cutter and AmCross would be sufficient to overcome any deficit in the event the BoB required an expanded Armour withdrawal.

- (ii) The CRCS contacted the BoB and requested further information regarding the British withdrawal. Dr. Boucher was advised that, based on available information, Dr. Perrault's opinion was that a full withdrawal of Armour AHF was warranted.

(c) On October 10, 1986, the CRCS took the following steps:¹⁶⁹⁹

- (i) The CRCS had a morning telephone conference with the BoB. Dr. Perrault reiterated that, given the availability of replacement heat-treated AHF, a full Armour withdrawal was viable and warranted. However, the BoB was hesitant to require a full withdrawal as this might lead to a worldwide shortage of heat-treated AHF. It noted that the FDA was requesting further information and had not yet made a decision about an Armour recall. The BoB advised the CRCS to hold off on any decision until the BoB consulted with the FDA. Dr. Perrault re-emphasized the CRCS position favouring a complete withdrawal of Armour heat-treated AHF and informed the BoB that the CRCS would require written instructions from BoB on this issue.

¹⁶⁹⁹ Ex. 660A, Vol. 58, Tab 25 (October 8 - 17, Handwritten Notes of Steven Vick and Dr. Tom Walker re: Discussions of Armour Withdrawal);

Ex. 660A, Vol. 58, Tab 26 (October 9, 1986, Memo from Dr. Leclerc-Chevalier, CBC to File);

Ex. 660A, Vol. 58, Tab 27 (October 10, 1986, Memo from Elaine Boily, Program Analysis, CBC File);
and

Ex. 647, Vol. 44, Tab 13 (October 29, 1986, Memo from Steven Vick to Dr. Perrault re: Armour Factor VIII Status Report).

- (ii) Immediately following the morning conference call, Dr. Perrault instructed Mr. Vick to purchase 10 million units of heat-treated AHF from Cutter as soon as possible in an effort to avert future shortages. Dr. Perrault contacted the CBC and informed it of this decision and Mr. Vick contacted Cutter and placed a firm order for replacement heat-treated AHF. The CRCS was concerned that, in the event the FDA issued an Armour recall, there would be a North American shortage of Factor VIII and replacement stocks would be difficult, if not impossible, to obtain.
- (iii) The CRCS also cancelled the delivery of six pending lots of Armour heat-treated AHF which amounted to approximately 12 million units.
- (iv) Tom Walker began notifying local CRCS Blood Centres about arrangements for replacement AHF.
- (v) The CRCS held an afternoon telephone conference with members of the BoB and Dr. Card representing the CHS MSAC. The BoB reiterated its concern and the concern of the FDA that a further withdrawal could seriously jeopardize the supply of heat-treated AHF. Dr. Card requested further information regarding the British withdrawal and Dr. Tom Walker re-emphasized the CRCS position that a total withdrawal was the preferred course of action. A decision was made that until additional information was obtained, no further action regarding an expanded withdrawal would be taken.
- (vi) Following the afternoon conference call, Dr. Perrault and Steven Vick informed the CBC of the current situation and Dr. Perrault once again expressed his concern regarding the need for a full Armour withdrawal.

- (d) On October 14, 1986, all CRCS local Blood Centres received replacement stocks for heat-treated Armour AHF and all shipments of Armour Factor VIII to hospitals were suspended.¹⁷⁰⁰
- (e) On October 15, 1986, the BoB received further information from Armour regarding the history of the two British hemophiliacs implicated in the recent Armour withdrawal. The information was inconsistent with information received earlier. Following a discussion between the CRCS, the BoB and Dr. Card, it was agreed to await further information from the FDA before making any decision regarding a full Armour withdrawal.¹⁷⁰¹
- (f) The CRCS also contacted two British experts, Dr. H. Gunson, an adviser on blood transfusion to the U.K. Department of Health and Social Security, and Dr. Chas Forbes, the Chair of the U.K. Hemophilia Centre Directors' Group, to obtain further information regarding the British seroconversions.¹⁷⁰²
- (g) On October 16, 1986, the FDA met and decided that all heat-treated AHF made from untested plasma from Armour would be withdrawn and that all product made from tested heat-treated AHF from Armour would not be withdrawn.¹⁷⁰³
- (h) On October 17, 1986, the BoB decided that, based on all available information, tested heat-treated AHF concentrate from Armour would not be withdrawn. In a faxed letter to Dr. Perrault, Dr. Furesz instructed the CRCS to continue distributing the product:

¹⁷⁰⁰ Ex. 647, Vol. 44, Tab 13 (October 29, 1986, Memo from Steven Vick to Dr. Perrault re: Armour Factor VIII Status Report).

¹⁷⁰¹ Ibid.

¹⁷⁰² Ex. 647, Vol. 44, Tab 12 (October 22, 1986, Memo from Dr. Davey to CRCS Medical Directors re: Armour AHF).

¹⁷⁰³ Ex. 647, Vol. 44, Tab 13, para. 6 (October 29, 1986, Memo from Steven Vick to Dr. Perrault re: Armour Factor VIII Status Report).

Following our review of the available scientific data, we concluded that the above product [Armour AHF], when prepared from plasma screened for HIV antibodies, is considered non-hazardous with respect to HIV infection in hemophilia patients. Consequently, we advise you to continue with the distribution of this product.¹⁷⁰⁴

Given that the BoB was responsible for issuing licenses and maintaining appropriate standards of safety for biological products, the CRCS felt obliged to follow the instructions of its regulator and continued to distribute tested heat-treated Armour AHF.¹⁷⁰⁵ In order to keep others informed of this decision, the CRCS sent copies of Dr. Furesz's correspondence to CHS representatives Dr. Card and Ed Gurney, Cutter and all CRCS Medical Directors.¹⁷⁰⁶

897. As a result of the reports and withdrawals discussed above, there was growing concern about the efficacy of the dry untested heat-treatment process. Despite the fact that no seroconversions or transmission episodes were linked with the Cutter process,¹⁷⁰⁷ the CRCS also undertook a voluntarily withdrawal of all Cutter untested heat-treated AHF (14 lots or approximately 2.2 million units of AHF). Dr. Davey contacted Dr. Card to obtain his assistance in informing members of the CHS MSAC of this voluntary Cutter withdrawal.¹⁷⁰⁸ Dr. Kaiser Ali, who succeeded Dr. Card as Chair of the CHS MSAC, later wrote with approval about this CRCS initiative:

¹⁷⁰⁴ Ex. 647, Vol. 44, Tab 8 (October 17, 1986, Letter from Dr. Furesz, BoB to Dr. Perrault re: Distribution of Armour AHF in Canada).

¹⁷⁰⁵ Evidence of Dr. Perrault, former National Director BTS, and Evidence of Dr. Davey, former Assistant National Director BTS, pp. 26975 - 26980.

¹⁷⁰⁶ Ex. 647, Vol. 44, Tab 8 (October 17, 1986, Letter from Dr. Furesz, BoB to Dr. Perrault re: Distribution of Armour AHF in Canada); and

Ex. 647, Vol. 44, Tab 12 (October 22, 1986, Memo from Dr. Davey to CRCS Medical Directors re: Armour AHF).

¹⁷⁰⁷ Evidence of Dr. Davey, former Assistant National Director BTS, pp. 26986 - 26987.

¹⁷⁰⁸ Ex. 648, Vol. 45, Tab 19 (February 19, 1987, Letter from Dr. Davey to Dr. Card).

Cutter kept selling products made from mixed lots because no regulatory agency asked for any recall. Following the March 1987 discovery of Cutter products derived from unscreened plasma, CRC talked with BoB and FDA about this issue. Because there were no reported cases of "breakthrough" seroconversions from Cutter products anywhere at that time, their product was considered safe by FDA. Despite the regulatory agencies' stance, CRC unilaterally withdrew the Cutter lots and paid for the replacement out of their own budget.¹⁷⁰⁹

898. The final blow to the Armour heat-treatment process occurred in the fall of 1987, when epidemiological data confirmed that Armour's *tested* heat-treated AHF was linked with the seroconversion of eight hemophiliacs in western Canada. As soon as the CRCS became aware of the seroconversions, it had discussions with the BoB and the CHS to formulate an action plan. Following these consultations, the CRCS took prompt and decisive measures to facilitate the recall of all lots implicated in the seroconversions. Details concerning CRCS efforts in this regard are set out below:

- (a) On October 20, 1987, the CRCS was advised by Dr. Kaiser Ali, then Chair of the CHS MSAC, that several hemophiliacs from western Canada had recently seroconverted. These patients had received heat-treated AHF from both Cutter and Armour and it was not immediately apparent which lots were responsible for the seroconversions. In order to clarify the situation and determine an appropriate response, Dr. McSheffrey, then CRCS Acting National Director of Blood Services, requested and obtained from the treating physicians the relevant data concerning AHF lot numbers and the serology results of the hemophilia patients.¹⁷¹⁰
- (b) On November 4, 1987, the CRCS met with the BoB and Dr. Leclerc-Chevalier. A decision was made to immediately replace all implicated lots of both Armour and Cutter

¹⁷⁰⁹ Ex. 770, Vol. 176, Tab 24, p. 055 (November 23, 1987, Memo from Dr. Kaizer Ali, Chair MSAC to All MSAC Members and Hemophilia Clinic Directors).

¹⁷¹⁰ Ex. 770, Vol. 176, Tab 8 (November 6, 1987, Memo from Dr. Kaiser Ali to MSAC Members and Hemophilia Clinic Directors); and

Ex. 650, Vol. 47, Tab 15 (October 26, 1987, Memo from Dr. McSheffrey to Steven Vick re: Recalls on Lots of Factor VIII).

AHF. Dr. Ali was contacted and concurred with the decision to take immediate action.¹⁷¹¹

- (c) Mr. Vick then contacted all CRCS Medical Directors advising of the product replacement and enclosing a list of Cutter and Armour lots implicated in the seroconversions. He noted that a considerable amount of the Cutter AHF had been the subject matter of the previous voluntary withdrawal of Cutter untested heat-treated AHF which took place in February, 1987. Out of an abundance of caution, these lots were nevertheless included in the November product replacement notice. It was also noted that the implicated Armour lots were all produced after the voluntary withdrawal of untested heat-treated Armour AHF in June of 1986. Medical Directors were instructed to follow standard recall procedures to ensure a prompt return of any remaining AHF from the implicated lots.¹⁷¹² The CRCS subsequently received information possibly implicating additional lots of Cutter and Armour AHF. In response, all CRCS Medical Directors received further replacement notices with instructions to immediately circulate this new information.¹⁷¹³
- (d) During the November 4, 1987 meeting with the BoB and Dr. Leclerc-Chevalier, Dr. McSheffrey communicated the decision of the CRCS to take immediate steps to convert

¹⁷¹¹ Ex. 770, Vol. 176, Tab 8 (November 6, 1987, Memo of Dr. Kaiser Ali to MSAC members and all Hemophilia Clinic Directors);

Ex. 651, Vol. 48, Tab 1, p. 67004 (November 5, 1987, Memo from Dr. McSheffrey to CRCS Medical Directors); and

Ex. 651, Vol. 48, Tab 6 (November 20, 1987, Memo from P. Tallieu to all CRCS Medical Directors and Commissioners).

¹⁷¹² Ex. 650, Vol. 47, Tab 15, p. 108468 (November 4, 1987, Memo from Steven Vick to CRCS Medical Directors re: Product Replacement).

¹⁷¹³ Ex. 650, Vol. 47, Tab 27 (November 13, 1987, Memo from Steven Vick to CRCS Medical Directors re: Product Replacement); and

Ex. 651, Vol. 48, Tab 4 (November 18, 1987, Memo from Steven Vick to CRCS Medical Directors re: Product Replacement).

to the newer enhanced virally inactivated factor concentrate. He indicated that all Canadian source plasma would, from that point on, be subject to the new wet heat or vapour treatment process.¹⁷¹⁴

- (e) On December 9, 1987, Dr. Robert Remis, an epidemiologist with the Federal Centre for AIDS, who was investigating the cause of the recent seroconversions, reported to representatives of the HPB and the FDA. Dr. Remis concluded that there was strong evidence linking the seroconversions with three lots of Armour heat-treated AHF.¹⁷¹⁵ This was communicated to the CRCS. On December 10, 1987, Mr. Vick notified all CRCS Medical Directors of this information and advised them to take immediate steps to ensure that all patients who may have received AHF from these lots were contacted:

Every effort is to be made through the hospitals and hemophilia treatment centres concerned, to contact TODAY all patients who received these product lots. (Emphasis original.)

Mr. Vick also indicated that, although there was no evidence of viral transmission by AHF of any other lots, returns of *any* AHF were to be accepted.¹⁷¹⁶

- (f) On December 11, 1987, the CRCS was notified by Armour of its decision to withdraw all lots of its AHF heat-treated at 60°C for 30 hours. Armour indicated that it had since revised its method of heat-treatment to a 68°C - 72 hour cycle. The CRCS immediately

¹⁷¹⁴ Ex. 650, Vol. 47, Tab 20 (November 4, 1987, Letter from Dr. McSheffrey to Dr. Leclerc-Chevalier, CBC re: Purchase of Advance Viral Inactivated Factor VIII).

Ex. 651, Vol. 48, Tab 1, p. 67004, para. 5 (November 5, 1987, Memo from Dr. McSheffrey to CRCS Medical Directors re: Factor VIII Replacement).

¹⁷¹⁵ Evidence of Dr. Remis, *Montreal Epidemiologist*, pp. 41306 - 41307.

¹⁷¹⁶ Ex. 651, Vol. 48, Tab 18 (December 10, 1987, Memo from Steven Vick to CRCS Medical Directors re: Product Recall).

contacted all its Medical Directors to advise that all Armour Factor VIII distributed by the CRCS was to be withdrawn.¹⁷¹⁷

- (g) Soon after the CRCS began the process of retrieving all available Armour AHF, the BoB upgraded the status of the Armour Factor VIII withdrawal to a formal recall. The BoB made this change once it was satisfied that a health hazard was established. All CRCS Medical Directors were advised of this information and were provided with copies of press releases issued by the Health Protection Branch and the FDA.¹⁷¹⁸
- (h) Dr. Furesz confirmed that the withdrawal of all Armour lots was completed by December 18, 1987.¹⁷¹⁹

b) CRCS Efforts to Secure Enhanced Virally Inactivated Factor Concentrate

899. The various problems associated with Armour's heat-treatment process only strengthened the CRCS resolve to ensure that a conversion to enhanced virally inactivated factor concentrate was carried out as soon as possible. As mentioned above, the CRCS presented its case for conversion to Dr. Leclerc-Chevalier on November 4, 1987,¹⁷²⁰ and began planning

¹⁷¹⁷ Ex. 651, Vol. 48, Tab 21 (December 11, 1987, Memo from Steven Vick to CRCS Medical Directors re: Product Withdrawal - Armour Pharmaceutical).

¹⁷¹⁸ Ex. 651, Vol. 48, Tab 20 (December 11, 1987, Memo from P. Tallieu to CRCS Medical Directors and Commissioners re: Recall of Armour Factor VIII). an;

Ex. 651, Vol. 48, Tab 22 (December 16, 1987, Memo from Steven Vick to CRCS Medical Directors re: Armour Factor VIII Recall).

¹⁷¹⁹ Ex. 771, Vol. 177, Tab 4, p. 16 (December 18, 1987, Memo from Dr. Furesz, BoB Circulated with a January 5, 1988 Memo from Dr. Kaiser Ali, Chair MSAC, to MSAC Members and Hemophilia Clinic Directors).

¹⁷²⁰ Ex. 650, Vol. 47, Tab 20 (November 4, 1987, Letter from Dr. McSheffrey to Dr. Leclerc-Chevalier re: Purchase of Enhanced Virally Inactivated Factor VIII); and

for implementation even without official ratification of this decision by the CBC.¹⁷²¹ In doing so, the CRCS overcame the external threat of a severe world-wide shortage of Factor VIII and managed to secure a supply of the safest, most technologically advanced factor concentrate for Canadian hemophiliacs.¹⁷²² Details concerning CRCS efforts in this regard are set out below.

900. During November 1987, the CRCS contacted fractionators to assess their ability to supply enhanced AHF as soon as possible. Given the concurrent withdrawals of dry heat-treated AHF, the CRCS recognized that the time to begin the conversion was "ripe".¹⁷²³ The CRCS kept the CBC informed about current information regarding the high cost and limited supply of enhanced AHF.

901. In a November 13, 1987 letter to Dr. Leclerc-Chevalier, Dr. McSheffrey estimated that the CRCS required approximately 30 million units of commercial AHF to satisfy hemophiliac needs for 1988. He noted that Immuno's vapour treated Factor VIII was licensed in Canada and was already being distributed by the CRCS in conjunction with the North American pilot study assessing the effectiveness of this new process on virgin hemophilia patients. However, beyond this, both Immuno and Cutter had only a few million units available

Ex. 651, Vol. 48, Tab 1, p. 67004, para. 5 (November 5, 1987, Memo from Dr. McSheffrey to CRCS Medical Directors re: Factor VIII Replacement).

¹⁷²¹ *Ex. 771, Vol. 177, Tab 4, p. 13 (January 5, 1988, Memo from Dr. Kaizer Ali, Chair MSAC, to MSAC Members and Hemophilia Clinic Directors).*

¹⁷²² *Ex. 772, Vol. 178, Tab 46 (April 18, 1989, Memo from Bill Mindell, Chair CHS Blood Resources Committee to Elaine Woloschuk and Bob Shearer re: Nomination of Steven Vick and Dr. Brian McSheffrey for Special Appreciation Awards at the 1989 Annual Meeting);*

Ex. 772, Vol. 178, Tab 50 (May 6, 1989, Report by Bill Mindell, Chair CHS Blood Resources Committee to CHS Annual Meeting); and

Evidence of Bill Mindell, CHS Member (Ontario Chapter), pp. 32364 - 32369.

¹⁷²³ *Evidence of Dr. Perrault, former National Director BTS, pp. 26993 - 26994.*

for purchase on a short term basis. Given the short supply situation and the anticipated expense involved in conversion, Dr. McSheffrey requested further direction from the CBC on an urgent basis.¹⁷²⁴

902. On November 27, 1987, Dr. Tom Walker provided members of the CRCS Blood Services Advisory Committee with an update on the supply situation. He noted that the CRCS was working closely with the CBC Executive Director and that an Ad Hoc Advisory Group was being formed with representation from the BoB and the CHS to advise the CRCS on issues related to the distribution of enhanced AHF.¹⁷²⁵

903. On December 7, 1987, Mr. Vick wrote to Dr. Leclerc-Chevalier providing a further update on the status of conversion to enhanced AHF. He confirmed that fractionators had insufficient capacity to satisfy Canadian requirements at present. However, he anticipated that complete conversion could be accomplished by April 1988. He pointed out that production of all dry heat-treated Factor VIII from CRCS plasma by Cutter had been suspended, awaiting further processing using the wet heat-treatment method as soon as additional capacity was available. He estimated a total conversion cost (including the cost to replace left over stocks of dry heat-treated AHF) to be \$27.7 million.¹⁷²⁶

904. By December 14, 1987, the CRCS had made arrangements to purchase approximately 3 million units of wet heat-treated concentrate from Cutter. This represented

¹⁷²⁴ Ex. 650, Vol. 47, Tab 26 (November 13, 1987, Letter from Dr. McSheffrey to Dr. Leclerc-Chevalier re: Factor VIII Costs and Yields).

¹⁷²⁵ Ex. 651, Vol. 48, Tab 11, p. 8, paras. 35 - 37 (November 27, 1987, Minutes of CRCS Blood Services Advisory Committee Meeting).

¹⁷²⁶ Ex. 651, Vol. 48, Tab 16 (December 7, 1987, Letter from Steven Vick to Dr. Leclerc-Chevalier re: Conversion to Wet Heat and Vapour Heat-Treated Factor VIII and IX).

approximately a one month supply for Canadian hemophiliacs¹⁷²⁷ and was expected to be available during the first three months of 1988.

905. On December 17, 1987, the CRCS Ad Hoc Committee on the Use of Factor VIII met via a telephone conference call to advise the CRCS on its distribution of wet and vapour treated enhanced AHF (hereinafter "enhanced"). Committee members included representatives from the CRCS, the BoB, the CBC, the CHS MSAC and the CHS Blood Resources Committee. Following a discussion about the different methods used by various fractionators, committee members strongly urged the CRCS to purchase additional enhanced AHF. They were satisfied that enhanced AHF offered the safest treatment option for hemophiliacs:

Evidence to date indicates wet or vapour processes are more efficient against NANB and are more likely to be effective against HIV. With respect to these products it is recommended that the Red Cross purchase and replace dry heat treated products with advanced viral inactivated products.¹⁷²⁸

Mr. Vick advised Committee members on the supply situation noting that the CRCS was in the process of purchasing an additional 4 million units of enhanced Factor VIII from Cutter. Contracts had been tentatively arranged with both Immuno and Cutter to satisfy supply requirements for 1988.

906. Given that only limited amounts of enhanced AHF would be available, committee members established priorities for use. Priority would be given to patients who had never received concentrates, patients known to be sero-negative for HIV and patients given only cryoprecipitate. Dr. Growe strongly urged the committee members that the distribution of the enhanced material be handled by the hemophilia treatment clinics. It was decided that (in

¹⁷²⁷ Ex. 770, Vol. 176, Tab 57 (December 14, 1987, Memo from Bob O'Neill, Chair CHS Task Force on HIV and AIDS, to CHS Chapter Presidents, Staff and National Board Members re: Blood Products Recall and Other Issues).

¹⁷²⁸ Ex. 770, Vol. 176, Tab 63, p. 158 (December 17, 1987, Minutes of the CRCS Ad Hoc Committee on the Use of Factor VIII Conference Call);

Ex. 770, Vol 176, Tab 72, (December 29, 1987, Telefax from Dr. McSheffrey to Mr. Mindell).

response to requests from hemophilia treaters) the CRCS would distribute the new AHF for use by patients who satisfied the protocol criteria. It was noted that Immuno was the only fractionator offering enhanced virally inactivated Factor IX although its process was not yet licensed in Canada.¹⁷²⁹

907. On December 21, 1987, Cutter wrote to Mr. Vick to guarantee supply of wet heat-treated Factor VIII for 1988. Cutter promised to supply 4 million units from CRCS plasma by the end of April 1988. Additional deliveries of 4.5 million units would follow every two months. In addition, Cutter would supply 10 million units of commercial units starting April 1, 1988. This would supplement the initial 3 million units negotiated in November 1987, the balance of which would be delivered as it became available until the end of April 1988. Cutter confirmed that it did not have any wet heat-treated Factor IX available for purchase.¹⁷³⁰

908. On December 29, 1987, Dr. McSheffrey provided all CRCS Medical Directors with an update regarding the status of conversion to enhanced AHF. He summarized the decision made at the December 17, 1987 Ad Hoc Committee on the use of Factor VIII. He noted that 4 million units of vapour treated and wet heat-treated Factor VIII would be available in the first three to four months of 1988. Given that the normal consumption for this period was approximately 14 million units, the limited supply of enhanced AHF was to be distributed only to patients satisfying the priority criteria established by the Ad Hoc Committee. He also noted that Immuno's enhanced Factor IX was expected to be licensed in early January 1988 and that by January 21, 1988 there would be sufficient material available for patients satisfying the priority criteria.¹⁷³¹

¹⁷²⁹ Ex. 770, Vol. 176, Tab 63, p. 158 (December 17, 1987, Minutes of the CRCS Ad Hoc Committee on the Use of Factor VIII Conference Call).

¹⁷³⁰ Ex. 651, Vol. 48, Tab 23 (December 21, 1987, Letter from Phil LeBlanc, General Manager, Cutter to Steven Vick).

¹⁷³¹ Ex. 651, Vol. 48, Tab 27 (December 29, 1987, Memo from Dr. McSheffrey to CRCS Medical Directors).

909. The CRCS continued to work closely with the CBC, the BoB and the CHS to implement conversion to enhanced AHF as soon as possible. This co-operative effort was acknowledged by Bill Mindell, Chair of the CHS Blood Resources Committee, in his January 1988 "Statement on the Safety of Factor VIII and Factor IX Concentrates in Canada":

You should also know that better products are on the way. Everyone involved in the Canadian blood system, including the CHS, has moved as rapidly as possible to acquire the new wet and vapour heat treated products which clinical experience indicates are safe with respect to HIV and also not known to transmit hepatitis viruses ... These improved products will begin to be distributed by the Red Cross in early January 1988 with a complete national replacement of all existing factor VIII and IX products expected by April 1988. Because of limited amounts of these products available on the world market at this time a priority system for allocation, which will apply equally across the country and has been agreed to by all parties involved, is necessary until there are enough supplies in the system to meet the needs of all who use factor products.¹⁷³²

910. In January 1988, the CRCS began issuing the limited amount of wet heat-treated AHF it had received from Cutter. These issues supplemented the Immuno vapour treated-AHF already being utilized in the virgin hemophiliac pilot study.¹⁷³³ Early in 1988, the CRCS foresaw a serious shortage of Factor VIII developing in the United States. It recognized that supply arrangements could become tenuous as fractionators abandoned the dry heat-treatment process and were faced with the significantly lower yields associated with enhanced AHF. The CRCS realized that, as pressure mounted for the U.S. fractionators to provide more enhanced AHF for the U.S. market, export restrictions could create a shortage in Canada. In order to avoid such a shortfall, the CRCS maintained regular contact with U.S. fractionators to assess the delicate supply situation.¹⁷³⁴

¹⁷³² Ex. 770, Vol. 176, Tab 71 (January 1988, Bill Mindell Statement on the Safety of Factor VIII and Factor IX Concentrates in Canada).

¹⁷³³ Ex. 652, Vol. 49, Tab 28, pp. 67295 and 67297 (National Factor VIII Inventory Documents re: Agenda Item #42, March 23 - 25, 1988 CRCS Medical Directors Meeting).

¹⁷³⁴ Ex. 653, Vol. 50, Tab 6 (April 14, 1988, Memo from Steven Vick to File re: Purchase of Hyland Monoclonal Factor VIII); and

Ex. 653, Vol. 50, Tab 30 (July 22, 1988, Letter from Dr. Whittemore, National Director, CRCS Blood Services to Dr. Leclerc-Chevalier re: World-Wide Shortage of Factor VIII).

911. Although it was not yet authorized by the CBC to issue purchase orders for additional enhanced AHF, the CRCS made "verbal agreements" in March 1988 with three fractionators to supply wet heat-treated, vapour treated and monoclonal Factor VIII. When the CBC complained about these unauthorized arrangements, the CRCS explained the desperate situation resulting from the world-wide shortage of Factor VIII and the need for prompt, decisive action to secure an adequate supply for Canadian hemophiliacs.¹⁷³⁵ On May 5, 1988, Dr. Perrault wrote to Dr. Leclerc-Chevalier defending CRCS efforts to keep the CBC informed while attempting to safeguard the interests of Canadian hemophiliacs:

The issue of a "perceived lack of consultation" between the Red Cross and the CBC was raised, concerning the purchase of factor VIII and the fractionation contract. I will admit that perhaps we had not worked out all the possible scenarios and options concerning a full analysis of needs and the availability of factor VIII during a market shortage worldwide. Our primary concern was to secure a source of supply and discuss the best possible options with the CBC without compromising the position of the funding governments. We had a sense of accomplishment in that regard i.e., that considerable amount of foresight was exercised by members of our staff at this time of difficult supply.

...

Since the issue of consultation had been raised repeatedly over the past five years, I felt some concern that our efforts to proceed on these two issues had raised the spectre of "lack of consultation"

... To our knowledge, we had done our best to fully inform your office and the members you represent.¹⁷³⁶

912. As a result of increased U.S. demand and the resulting shortage, the CRCS was unable to obtain sufficient supplies of enhanced AHF to meet its original forecast for full conversion by April 1988. Nevertheless, the CRCS continued its efforts to obtain as much enhanced AHF as possible as soon as possible.

¹⁷³⁵ Ex. 653, Vol. 50, Tab 14, para. 64 (April 26, 1988, Memo from Dr. McSheffrey to File re: April 21 - 22, 1988 Meeting with the CBC).

¹⁷³⁶ Ex. 653, Vol. 50, Tab 18 (May 5, 1988, Letter from Dr. Perrault to Dr. Leclerc-Chevalier re: April 21 - 22, 1988 CBC Meeting).

913. In early June 1988, the CRCS requested permission from the CBC to formalize its prior verbal agreements with the U.S. fractionators. Permission was granted, and by mid-June 1988, the CRCS issued purchase orders for wet heat-treated and vapour treated Factor VIII.¹⁷³⁷ On the strength of the supplies that it received from the U.S. fractionators, the CRCS was able to fully convert to enhanced AHF by July 11, 1988. As of that date, the CRCS stopped issuing dry heat-treated concentrate, except for limited circumstances when hemophiliacs, who preferred the dry heat-treated material, specifically requested it.¹⁷³⁸

914. Throughout the summer of 1988, the CRCS unsuccessfully attempted to obtain additional supplies of wet heat-treated Factor VIII. It did, however, have a verbal agreement with Hyland for the purchase of monoclonal Factor VIII to satisfy projected patient requirements until the end of the CRCS fiscal year. Monoclonal Factor VIII was substantially more expensive (60¢ U.S. per unit) than either wet heat-treated (30¢ - 40¢ U.S. per unit) or vapour treated Factor VIII (40¢ U.S. per unit). In light of the current supply situation, the only alternative to purchasing the more expensive monoclonal Factor VIII was to revert to the use of fresh frozen plasma and cryoprecipitate. This form of treatment was widely regarded as much less safe than the use of enhanced AHF, and, as Dr. Whittemore pointed out to Dr. Leclerc-Chevalier, such a move would be perceived as a "desperate third world solution" by Canadian hemophiliacs.¹⁷³⁹ In light of the precarious supply situation, the CBC authorized the CRCS to issue a purchase

¹⁷³⁷ Ex. 653, Vol. 50, Tab 30 (July 22, 1988, Letter from Dr. Whittemore, National Director, CRCS Blood Services to Dr. Leclerc-Chevalier re: World-Wide Shortage of Factor VIII).

¹⁷³⁸ Ex. 654, Vol. 51, Tab 11, p. 17754, para. 20 (October 25, 1988, Minutes of the CBC Advisory Sub-Committee); and

Ex. 654, Vol. 51, Tab 20, p. 71873 (CRCS Position Paper re: Status of Factor VIII Supply in Canada for Agenda Item #6, November 14, 1988 CRCS National Blood Services Committee Meeting).

¹⁷³⁹ Ex. 653, Vol. 50, Tab 30, p. 20993 (July 22, 1988, Letter from Dr. Whittemore to Dr. Leclerc-Chevalier re: World-Wide Shortage of Factor VIII).

order for 9 million units of Hyland's monoclonal Factor VIII. This new process was licensed by the BoB on September 21, 1988 and the CRCS received its first shipment in late October 1988.¹⁷⁴⁰

915. In an effort to provide greater certainty and stability of supply, the CRCS negotiated a five year contract with Cutter for enhanced AHF derived from CRCS plasma. The CBC recognized that such a long term contract would ensure a secure and safe supply of factor concentrate while providing a substantial cost savings to the Canadian blood program (\$25 million in the first year of the contract). As a result, the CBC authorized the CRCS to enter into the five year fractionation contract with Cutter.¹⁷⁴¹

8) CRCS Officials Awarded For its Action

916. As a result of the various measures described above, the CRCS helped ensure a rapid transition to enhanced AHF. In co-operation with the CBC, the BoB and the CHS, the CRCS took the necessary action to secure a supply of state-of-the-art AHF without any interruptions in domestic supply despite a world-wide shortage of Factor VIII. The significance of this accomplishment was gratefully acknowledged by CHS board members who presented Mr. Vick and Dr. McSheffrey with special appreciation awards at the CHS 1989 Annual Meeting.¹⁷⁴² The CRCS officials were nominated by Mr. Mindell, the Chair of the CHS Blood

¹⁷⁴⁰ Ex. 654, Vol. 51, Tab 3 (September 30, 1988, Letter from Dr. Leclerc-Chevalier to Dr. Whittemore re: Hyland Monoclonal Factor VIII); and

Ex. 654, Vol. 51, Tab 20, p. 71873 (CRCS Position Paper re: Status of Factor VIII Supply in Canada for Agenda Item #6, November 14, 1988 CRCS National Blood Services Committee Meeting).

¹⁷⁴¹ Ex. 654, Vol. 51, Tab 23 (November 24, 1988, Letter from Dr. Leclerc-Chevalier to Dr. Whittemore re: Plasma Fractionation Contract).

¹⁷⁴² Evidence of Bill Mindell, CHS Member (Ontario Chapter), pp. 32364 - 32369; and

Ex. 772, Vol. 178, Tab 46 (April 18, 1989, Memo from Bill Mindell, Chair, CHS Blood Resources Committee to Elaine Woloschuk and Bob Shearer re: Nomination of Steven Vick and Dr. McSheffrey for Special Appreciation Award at the 1989 Annual Meeting).

Resources Committee, and Dr. Kaiser Ali, the Chair of CHS MSAC. In a memo supporting these nominations, Mr. Mindell emphasized the "unprecedented co-operation" between the CRCS and the CHS which facilitated implementation of the new enhanced AHF despite significant obstacles:

These objectives were achieved despite the absence of a Canadian Blood Policy and resistance, and confusion, about the acquisition of new blood products at high levels in the governments of Canada.¹⁷⁴³

917. In summarizing the various accomplishments, Mr. Mindell highlighted the "immediate withdrawal" of all suspect lots following the 1987 seroconversions in western Canada and the "rapid acquisition" of enhanced AHF despite severe shortages in the U.S. and elsewhere. Commenting on CRCS foresight to quickly acquire sufficient supplies of enhanced AHF, Mr. Mindell noted:

Few Canadian with hemophilia noticed the "shortage" at all. This achievement was nothing short of superb strategic and operational management from the CRC BS.¹⁷⁴⁴

Mr. Mindell concluded his nomination memo by stressing the dedication and professionalism of the CRCS officials who worked hard to protect the health and safety of Canadian hemophiliacs:

It is important to realize that none of the above accomplishments happened by accident and that there were many forces, in Canada and externally, that operated against these outcomes. Many individuals worked hard and they worked together to achieve these goals, but these achievements would not have been possible without the extraordinary professional skills, commitment, determination, dedication and willingness to take risks on behalf of Canadian Hemophiliacs of Dr. Brian McSheffrey and Stephen Vick of the CRC BS. It was their handling of their responsibilities that turned the dangerous situation we faced into a triumph from which we have benefitted so greatly. Both Mr. Vick,

¹⁷⁴³ Ex. 772, Vol. 178, Tab 46 (April 18, 1989, Memo from Bill Mindell, Chair, CHS Blood Resources Committee to Elaine Woloschuk and Bob Shearer re: Nomination of Steven Vick and Dr. McSheffrey for Special Appreciation Award at the 1989 Annual Meeting).

¹⁷⁴⁴ *Ibid.*

Director of Blood Products, and Dr. McSheffrey, a hemophilia treater who temporarily filled the post of Acting Director of the CRC BS, were relatively new in their positions; Dr. McSheffrey has since returned to his former position.

I wish to nominate these two individuals for special awards from the CHS, either "distinguished service" or "special appreciation" plaques, for their dedicated service and commitment to insuring [sic] that the best possible blood products are available to Canadians with hemophilia.¹⁷⁴⁵

9) Conclusion

918. The CRCS overcame numerous obstacles to acquire and implement heat-treated AHF. Various regulatory problems and market forces outside of the control of the CRCS threatened its ability to secure a stable supply of this new form of concentrate. From November 1984 when the BoB issued its directive until July 1985 when full conversion was reached, the CRCS worked closely with the fractionators, CBC, the BoB and the CHS to ensure heat-treated AHF was implemented as soon as possible. The CRCS faced similar challenges when it initiated a conversion to enhanced virally inactivated factor concentrate. Through a co-operative effort, implementation was also completed within an eight month period (November 1987 - July 1988). Given the similar time frames and circumstances, it is difficult to understand why the CRCS has been criticised for its implementation of heat-treated AHF and yet praised for its implementation of enhanced AHF. In both cases, CRCS officials and medical staff strove to obtain and distribute the safest factor concentrate available.

¹⁷⁴⁵ *Ibid.*

G. RECALLS AND WITHDRAWALS

1) Development of a National Recall Policy

919. The health and lives of hemophiliacs were endangered by a bleed. As it was essential to ensure that an adequate supply of concentrates was available to treat such bleeds, the position of the CRCS, fractionators and the BoB on recalls and the withdrawal of product was based upon a risk-benefit consideration.

920. Drs. Zuck and Eyster, in their recent address to the IOM Report, commented about the need to be cognizant of the critical shortages and devastating effect a shortage of AHF would have on the hemophilia community:

The Report assumes, without critical examination of the issue, that recalls of factor VIII would have been beneficial. In addressing recalls of antihemophilic factor (AHF) concentrates, the Report incompletely discusses the issues of adequate supply that were of great concern to all involved. As late as 1988, only 125 to 175 million units of heat-treated AHF concentrates were available in the United States, at a time when the demand was as high as 350 million units. In 1982, hemorrhage, especially in the central nervous system, remained by far the most common cause of death in hemophiliacs, accounting for 48 percent of deaths and a 30-percent increase in morbidity over that among men in the general US population. An analysis of these data does not appear in the Report.¹⁷⁴⁶

921. Historically, in the case of single donor blood components, if the CRCS was alerted that a donor was suffering from a transmissible disease the CRCS would trace that donation to a hospital blood bank and withdraw any components associated with that donor.¹⁷⁴⁷ In cases which involved manufactured pooled plasma products, namely concentrates, the

¹⁷⁴⁶ Ex. 1299 (Zuck, T.F. and Eyster, M.E. "Blood and safety decision, 1982 to 1986: perceptions and misconceptions.", Transfusion, October 1996).

¹⁷⁴⁷ See Section III.H. Lookback/Traceback.

initiation of a recall or withdrawal due to the *possibility* of a health risk was a more difficult and complicated matter. The CRCS developed policies in concert with the BoB to address this situation.

922. In 1981, the BoB and the CRCS discussed guidelines on the procedure in situations where plasma in the process of fractionation was linked to a donor or to a recipient who subsequently developed hepatitis. In such cases, one bad donation could theoretically "spoil the pot":

It was recognized that situations where several donors and possibly multiple lots of plasma may be involved have the potential of seriously affecting the delivery of plasma fractionation products.¹⁷⁴⁸

923. Regulations required that blood and blood components be tested and found negative for HBsAg prior to issue or processing. However, because of the limitations of the test, blood banks continued to monitor hepatitis in donors and post-transfusion hepatitis in a recipient. It was determined that in cases where a donor subsequently developed hepatitis or where hepatitis was discovered in a recipient, every effort would be made to prevent further use of the component plasma or fractionation products associated with the donor by either preventing suspect units of plasma from being pooled or, where the plasma had already been pooled, by withdrawing or recalling the product.¹⁷⁴⁹ Where a decision was required as to whether to withdraw or recall a possibly contaminated product, the BoB and the CRCS would consider what constituted the greater threat to the consumers: the loss of the concentrate as a therapeutic agent and potentially life-saving biological product, or the risk of contracting hepatitis.¹⁷⁵⁰ This determination called for communication between the BoB, the CRCS and the fractionator.¹⁷⁵¹

¹⁷⁴⁸ Ex. 750, Vol. 157, Tab 63, p. 243 (*Minutes of Bureau of Biologics and Canadian Red Cross Meeting held July 13, 1981*).

¹⁷⁴⁹ *Ibid*, pp. 243-244.

¹⁷⁵⁰ *Ibid*, p. 244

¹⁷⁵¹ Ex. 613, Vol. 10, Tab 10 (*September 24, 1981 Memorandum from Dr. Derrick to Dr. Perrault*);

Evidence of Dr. Davey, former Assistant National Director BTS, p. 26488; and

924. This balancing of the risk versus benefit had precedent in other biological products (e.g. vaccines).¹⁷⁵² The accepted policy was that where there was an abundance of supply, the prudent course was to recall or destroy the concentrates if plasma production was in mid-process.¹⁷⁵³

a) The Advent of AIDS - U.S. Recall Policies

925. In 1983, U.S. Federal health officials and representatives of the fractionators met to determine a course of action with regard to recalls in cases in which concentrate lots were found to contain plasma from a donor who had subsequently developed AIDS. There was an overriding concern about the possibility of "drying up" the world AHF supply, which would put hemophiliacs in jeopardy.¹⁷⁵⁴ The FDA summarized the dilemma:

It was very clear that confronted with this complex problem, the Committee felt that a balance must be struck between theoretical risk of the product to recipients against the need for an uninterrupted supply of life-sustaining therapy.¹⁷⁵⁵

926. It was determined that a lot which incorporated plasma from a donor with a *definite* diagnosis of AIDS would mandate a recall. A lot, however, containing plasma from a donor with signs or symptoms merely *suggestive* of AIDS would not be persuasive enough to dictate a recall. The consensus of the FDA Blood Products Advisory Committee was that cases relating to donors with signs or symptoms merely suggestive of AIDS should be determined on a case-by-case basis.¹⁷⁵⁶

Ex. 621, Vol. 18, Tab 38 (October 12, 1983, Memorandum to Dr. Davey from Dr. Naylor re: Cutter Factor VIII Concentrate, Lot CW8028).

¹⁷⁵² *Evidence of Dr. Perrault, former National Director BTS, p. 26485.*

¹⁷⁵³ *Evidence of Dr. Perrault, former National Director BTS, p. 26486.*

¹⁷⁵⁴ *Ex. 931, Vol. 228, Tab 2, p. 46851 (July 19, 1983, "Trip Report").*

¹⁷⁵⁵ *Ex. 555, Vol. 128, Part 2, Tab 32, p. 168 (July 19, 1983, Blood Products Advisory Committee Summary Minutes).*

¹⁷⁵⁶ *Ibid, pp. 168-169.*

927. This policy continued into the fall of 1984 and early 1985. During this time, it was not known whether all lots of AHF concentrate were, indeed, infected with the HIV virus. The October 1984 recommendation of the NHF in reference to the use of heat-treated concentrates was by no means absolute:

We do not yet have sufficient data of scientific nature to know with certainty that viral attenuated (heat-treated) coagulation factor concentrates should now be universally adopted. However, very preliminary data do suggest that HTLV-III is heat sensitive. Further, we do not know whether hemophiliacs who are positive for antibody to HTLV-III have been exposed to living virus capable of causing AIDS, or have developed effective immunity against AIDS.

...

We reaffirm our position that patients continue treating bleeding episodes with clotting factor as prescribed by their physicians, as the risks of withholding treatment far outweigh the risks of treatment.¹⁷⁵⁷

928. On May 8, 1985 NHF MSAC revised its policy. Its recommendation was that where a *non*-heat-treated product contained plasma from a donor who was subsequently diagnosed with AIDS or, in the best judgment of the manufacturer, had characteristics strongly suggestive of AIDS, all lots associated with the donation were to be withdrawn. If, however, lots had been heat-treated and contained a donation from a donor who subsequently developed AIDS, MSAC was *not* advising that the lots be withdrawn. At no time did the NHF MSAC generically recommend that non-heat-treated concentrates should be withdrawn.¹⁷⁵⁸

¹⁷⁵⁷ Ex. 758, Vol. 164, Tab 25, p. 105 (October 13, 1984, *Hemophilia Information Exchange, AIDS Update*).

¹⁷⁵⁸ Ex. 743, Tab 14 (May 8, 1985 *Hemophilia Information Exchange, AIDS Update*).

b) Connaught Recalls: 1983

929. The CRCS always had mechanisms in place for the speedy and swift recall of plasma derivatives or blood components. With the advent of AIDS and the corresponding fears concerning AIDS in the blood supply in the 1980s, there were more frequent lot recalls of concentrates. One of the first and most notable recalls occurred in August, 1983.¹⁷⁵⁹

930. On August 23, 1983, Dr. Pearson of Connaught telephoned the CRCS to advise that Connaught wished to voluntarily withdraw a number of its vials of factor VIII concentrate.¹⁷⁶⁰ The CRCS protocol in place at this time enabled it to make immediate contact with its centres to initiate the recall procedure.

931. Craig Anhorn, the manager of Blood Products Services, immediately telephoned the three BTS Centres (London, Hamilton, and Toronto) who had received the concentrate, and explained the reasons for the recall, product lots involved and:

the need to fully reconcile the amount of product issued to hospitals with any that hospitals would return from stocks or as result of contacting patients to whom product had been issued.¹⁷⁶¹

On August 24, 1983, written memos were sent to London, Hamilton and Toronto Centres by Dr. Naylor, confirming this information.¹⁷⁶²

¹⁷⁵⁹ *Evidence of Dr. Davey, former Assistant National Director BTS, pp. 26448-26449;*

Ex. 620, Vol. 17, Tab 40 (August 23, 1983, Letter to Dr. Davey from J. Weber); and

Ex. 620, Vol. 17, Tab 41 (August 24, 1983, Memos to Medical Directors and Technical Supervisors - Hamilton Centre, Toronto Centre and London Centre re: Recall of Connaught Factor VIII).

¹⁷⁶⁰ *Ex. 621, Vol. 18, Tab 39 (October 14, 1983, Memorandum to Dr. Perrault from Dr. Naylor re: Recalls of Connaught Factor VIII Supplementary Purchases).*

¹⁷⁶¹ *Ibid, p. 75543.*

¹⁷⁶² *Ibid, p. 75543; and*

Ex. 620, Vol. 17, Tab 41 (August 24, 1983, Memos to Medical Directors and Technical Supervisors - Hamilton Centre, Toronto Centre, and London Centre re: Recall of Connaught Factor VIII).

932. The CRCS National office traced the number of vials issued to each of the Centres. For example, Hamilton Centre had received a total of 480 vials of the lots in question,¹⁷⁶³ Toronto Centre had received 1,067 vials,¹⁷⁶⁴ and Ottawa Centre had received 750 vials.¹⁷⁶⁵ Dr. Naylor requested that each of the centres facilitate a "complete reconciliation of all vials" and forward to National office a detailed listing of the number of vials of each lot issued to each hospital and the number of vials returned.¹⁷⁶⁶ Dr. Naylor provided the centres with the information he had as to the reason behind these voluntary withdrawals by Connaught:

This action has been taken because one of the plasmapheresis centres from which Connaught obtains fresh frozen plasma, found that two donors failed to inform the centre that they had had hepatitis about five years ago.¹⁷⁶⁷

933. On August 24, 1983, Ed Gurney, the Executive Vice-President of the CHS, contacted Dr. Naylor to ask for information on the reasons for the recall as "his office had been inundated with calls from patients who thought that the recall had been because of AIDS."¹⁷⁶⁸ Thus, it is apparent that the BTS Centre recalls had been immediately instituted.

934. The CHS complained that communication between the CRCS and its organization was poor as it had not been directly contacted about the recall. Dr. Naylor commented that representation by a member of the BTS on the CHS MSAC, already under consideration by the CHS MSAC, would resolve this shortcoming.¹⁷⁶⁹

¹⁷⁶³ *Ibid*, p. 75659.

¹⁷⁶⁴ *Ibid*, p. 75661.

¹⁷⁶⁵ *Ibid*, p. 75663.

¹⁷⁶⁶ *Ibid*, p. 75659.

¹⁷⁶⁷ *Ibid*, p. 75659.

¹⁷⁶⁸ *Ex. 620, Vol. 17, Tab 43 (August 25, 1983, Memorandum to File from D.H. Naylor re: August 24, 1983 Telephone Conversation with Ed Gurney).*

¹⁷⁶⁹ *Ibid*.

935. On August 24, 1993, Dr. Herst, in her capacity as Chair of the Ontario MSAC, issued a notice concerning the recall on CHS letterhead,¹⁷⁷⁰ which outlined the lots involved and the reason behind the recalls. She wrote:

The blood bank from which you obtain your coagulation products should have notified you about the recall. Return any unused vials of these lot numbers to your blood bank.¹⁷⁷¹

936. On August 25, 1983, the Hamilton Niagara Regional Hemophilia Centre sent the following memo to hemophilia patients informing them of the recall of the Connaught lots which stated:

If you have in your possession any of this Factor VIII, please do not use it and return these lots to the hospital at your earliest convenience.¹⁷⁷² [Emphasis original]

937. On September 2, 1983, Connaught contacted the CRCS to request the voluntary recall of two additional lots of Factor VIII concentrates made from the plasma from two donors who had hepatitis.¹⁷⁷³ On that day, the BTS telephoned London, Hamilton, and Toronto CRCS centres to inform them of the recall and its reasons.¹⁷⁷⁴

938. On September 2, 1983, CRCS National staff telephoned Ed Gurney of the CHS to inform him of the latest recall.¹⁷⁷⁵ In the CRCS recall notices, Medical Directors were

¹⁷⁷⁰ Ex. 754, Vol. 160, Tab 69 (August 24, 1983, Important Notice for Hemophiliacs Using Factor VIII Concentrate).

¹⁷⁷¹ Ibid, Tab 69.

¹⁷⁷² Ex. 754, Vol. 160, Tab 71 (August 25, 1983, Hamilton Niagara Regional Hemophilia Centre Notice "To All Hemophilia Patients").

¹⁷⁷³ Ex. 621, Vol. 18, Tab 39, p. 75543 (October 14, 1983, Memorandum to Dr. Perrault from Dr. Naylor re: Recalls of Connaught Factor VIII Supplementary Purchases). This was supplementary plasma purchased by Connaught from U.S. prisons without the knowledge of the CRCS.

¹⁷⁷⁴ Ibid, p. 75544.

¹⁷⁷⁵ Ex. 621, Vol. 18, Tab 8 (September 6, 1983 Memorandum from Dr. Naylor to File Re: Connaught Laboratories (CLL) Request for Product Recall Factor VIII Concentrates Lots 36226, 36227).

instructed to notify the treating physicians in the area and to outline the reasons behind the recall, "so that they are prepared to offer appropriate advice to any of their patients who have used concentrate from these batches."¹⁷⁷⁶

939. In the course of the recalls of the Connaught lots, there were some breakdowns in the chain of communication. For example, on September 6, 1983, the parents of a hemophiliac received a copy of Dr. Herst's August 24, 1983 recall notice from the CHS Ontario Chapter. Unfortunately, neither the patient nor his family had been contacted by the blood bank of the Children's Hospital of Eastern Ontario or Connaught Laboratories.¹⁷⁷⁷ The matter was immediately investigated by the CRCS at the request of the CHS Ontario Chapter.¹⁷⁷⁸

940. Dr. Rock, of the Ottawa Centre, responded to the inquiries concerning this breakdown in communication. Ottawa Centre confirmed that it had informed all hospitals of the recall by telephone within four hours of the receipt of the information from National office on August 23, 1983. The hospitals were again telephoned on August 24, 1983, at which time specific details concerning the recall were provided. Finally, a formal letter went out on August 29, 1983, from the Ottawa Centre to all hospitals.¹⁷⁷⁹ While communication between the Ottawa CRCS and the hospital blood banks was prompt and efficient, it was noted that:

Subsequent communication between hospitals and treating physicians would seem to be inadequate, but this is beyond the direct jurisdiction of the BTS.¹⁷⁸⁰

¹⁷⁷⁶ Ex. 621, Vol. 18, Tab 7 (September 6, 1983, Memorandum to Dr. Barr and Dr. Zuliani from Dr. Naylor re: Recall of Factor VIII Concentrates).

¹⁷⁷⁷ Ex. 755, Vol. 161, Tab 16 (September 9, 1983 Letter from Ms. Harper re: Important Notice for Hemophiliacs Using Factor VIII Concentrate).

¹⁷⁷⁸ Ex. 755, Vol. 161, Tab 23 (September 15, 1983 Memorandum from Dr. Naylor to Dr. Rock re: Recall of Connaught Factor VIII Lots 36233-1, 36238-1).

¹⁷⁷⁹ Ex. 755, Vol. 161, Tab 24 (September 19, 1983, Letter to Dr. Naylor from Dr. Rock).

¹⁷⁸⁰ Ex. 621, Vol. 18, Tab 33 (October 6, 1983, Letter to Ms. Harper from Dr. Naylor re: Recall of Connaught Factor VIII Lots).

941. While prompt CRCS action ensured that recall information was rapidly transmitted from National Office to centres, hospital blood banks, and treating physicians,¹⁷⁸¹ the "weak link in the chain" appeared to be in the communication between hospitals, treating physicians and patients. While this was beyond the jurisdiction of the CRCS, it worked with the CHS to help ensure that communication between these groups improved.

942. The CHS MSAC requested that the Ontario and National MSACs make recommendations concerning blood recalls, particularly as they related to the communication from the hospital perspective once it was informed by the local BTS.¹⁷⁸² On November 10, 1983, Joanne Harper wrote to Ed Gurney, of the CHS, recommending that its national MSAC develop an informational update to be used in the event of blood recalls. The national CHS was to produce a labelled mailing list of Canadian recipients of concentrates that could be utilized in the event of a recall:

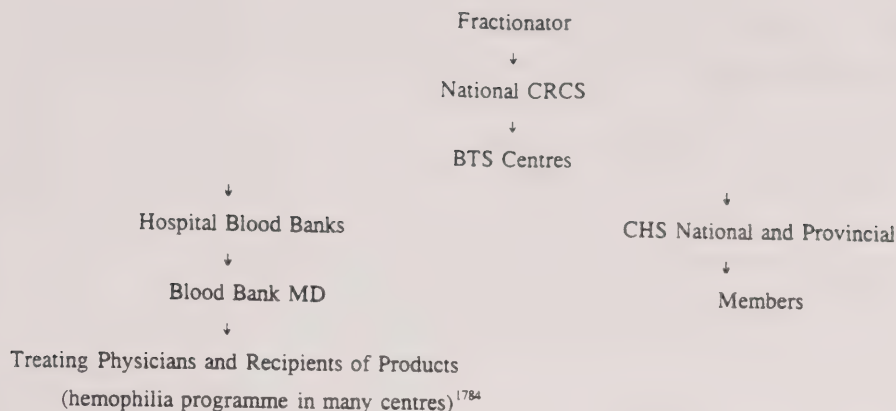
In the meantime, in Ontario, our MSAC will work on the task of clarifying recall procedures with hospital blood banks, to ensure better notification through designated channels.¹⁷⁸³

943. On November 15, 1983, Dr. Herst wrote to Dr. Naylor concerning product recalls. She suggested procedures to minimize the delays and noted the communication chain was as follows:

¹⁷⁸¹ *Ibid.*

¹⁷⁸² *Ex. 755, Vol. 161, Tab 46, p. 1349 (October 18, 1983, Memorandum to Dr. Herst from Joanne Harper).*

¹⁷⁸³ *Ex. 755, Vol 161, Tab 64, p. 01361 (November 10, 1983, Memorandum to Ed Gurney from Ms. Harper re: Cutter Recall of Factor VIII and IX Concentrates).*



944. Dr. Herst suggested that when National BTS received information about a product recall:

...a concise, factual notice should be prepared, on letterhead or special note form, dated, with wording appropriate to a non-medical person. Enough information about reasons should be provided with due regard to legal implications. This notice could then be sent to the Centres along with a separate covering memo and any additional information necessary for the Centres. The notice could be reproduced by the Centres and sent to the hospitals and the hospital blood bank could send the same notice to the involved physicians and patients.¹⁷⁸⁵

945. Dr. Herst recognized that communication problems in the hospital blood banks were often related to poor record-keeping at the hospital level.¹⁷⁸⁶ It was hoped that a uniform informational notice might "lessen the time required to disseminate such information from hospitals to users".¹⁷⁸⁷

¹⁷⁸⁴ *Evidence of Dr. Herst, Toronto Centre Medical Director, pp. 34133-34135; and*

Ex. 755, Vol. 161, Tab 65, p. 168 (November 15, 1983 Memorandum from Dr. Herst to Dr. Naylor re: Communication About Fractionation Recall).

¹⁷⁸⁵ *Ibid, p. 168.*

¹⁷⁸⁶ *Ibid, p. 168.*

¹⁷⁸⁷ *Ex. 755, Vol. 161, Tab 71 (November 24, 1983, Memorandum to Dr. Wrobel and Dr. Herst from Dr. Naylor).*

946. In December 1983, Dr. Naylor corresponded with Ken Poyser concerning the existing recall procedure and discussed its draft proposal for handling recalls:

Essentially it is a refinement of the procedure that the NBTS has used recently, but with certain improvements that should ensure the dissemination of information in a more uniform way...

... in order to be effective, will require more efficient lines of communication between hospital blood banks, hemophilia treatment physicians and their patients. The National and Provincial CHS can play a major role at this level in expediting product recall.¹⁷⁸⁸

947. A draft recall policy document was reviewed at the CRCS Blood Components Working Group in April 1984.¹⁷⁸⁹ In the interim, the CRCS continued its general procedure outlined above and co-operated with the CHS to alleviate concerns about poor communication. In December 1983, Dr. Naylor commenced his membership on the National MSAC as the CRCS representative.¹⁷⁹⁰ This enabled communication between the CRCS and Canadian hemophilia treaters on issues of concentrate changes, distribution, recalls and policy changes that would impact on the distribution of plasma derivatives in Canada.¹⁷⁹¹

c) Recall Policy: Commercial Manufacturers

948. In the United States over the course of 1983, a number of commercially produced lots of concentrate were recalled by fractionators in the wake of reports that plasma donors contributing to the pools had later developed AIDS. These recalls were restricted entirely to the United States and did not affect the Canadian supply. Nevertheless, in light of these recalls, the CRCS determined that greater vigilance was required. It sought assurances that fractionators

¹⁷⁸⁸ Ex. 755, Vol. 161, Tab 79, pp. 200-201 (December 15, 1983, Letter to Ken Poyser from Dr. Naylor Re: Approaches to Achieving Self-Sufficiency in Factor VIII Concentrate).

¹⁷⁸⁹ (This is discussed in subsection e)).

¹⁷⁹⁰ Ex. 755, Vol. 161, Tab 82, p. 221 (December 19, 1983, Memorandum to All MSAC Members and Consultants from Dr. Strawczynski).

¹⁷⁹¹ See Section III. E. - CRCS Relationship Between Hemophilia and Hemophilia Treaters.

utilized an effective recall policy enabling immediate identification and retrieval of any potentially contaminated lots.

949. Accordingly, in 1983 in the face of Connaught recalls and the U.S. situation, the CRCS included the following requirement:

The quote must further specify the supplier's product recall policy and procedure to be undertaken, should any lot be found to have been produced from a pool containing one or more units of unacceptable plasma.¹⁷⁹²

950. Of the five quotations received by the CRCS in 1983 for the 1984 year, only three fractionators (Cutter, Fenwal and Armour) provided recall information. Fenwal, however, did not disclose the source of the plasma used in their concentrates; Cutter and Armour were awarded the contract.¹⁷⁹³ These requirements were included in all subsequent CRCS RFPs to supply commercial concentrate and served to further safeguard the Canadian blood supply.¹⁷⁹⁴

d) HPB Recall Policy

951. The CRCS and the manufacturers were not the only parties in the blood system involved in product recalls. The HPB had drafted its own product recall protocol.¹⁷⁹⁵ Up until

¹⁷⁹² Ex. 621, Vol. 18, Tab 26, p. 43445 (CRCS BTS Request for Proposal: Anti-hemophilic Factor [AHF] Concentrate).

¹⁷⁹³ Ex. 622, Vol. 19, Tab 14, p. 50257 (1984 AHF Concentrate RFP, November 9, 1983);

Ex. 622, Vol. 19, Tab 21, p. 066216 (November 15, 1983, Letter to Phil LeBlanc from Martin Davey re: RFP 0006-83); and

Ibid, p. 50262 (November 15, 1983, Letter to Mr Greenwell from Martin Davey).

¹⁷⁹⁴ Ex. 629, Vol. 26, Tab 9, pp. 38159-38171 (RFP 006-84); and

Ex. 640, Vol. 37, Tab 30, p. 035739 (RFP 006-85).

¹⁷⁹⁵ Ex. 623, Vol. 20, Tab 30 (January 1, 1984, Product Recall Procedures, Health and Welfare Canada).

1984, the HPB had been involved in approximately 200 recalls of food, drugs, cosmetics, and devices in Canada:

These recalls have been carried out by the manufacturers, distributors, retailers and importers... The primary role of the Health Protection Branch during such recalls is to closely monitor the effectiveness of the firm's recall actions and to provide scientific, technical and operational advice. In crisis situations, our inspectors and those of other health agencies are also directly involved in physically removing products from further sale and the Branch takes a lead role in alerting the public through the news media.¹⁷⁹⁶

952. If a firm's recall performance was inadequate, the HPB could take appropriate action to remove the product from sale or use. Moreover, a firm's recall actions did not preclude further enforcement actions being taken by the BoB, as deemed appropriate, either during or following the completion of the recall.¹⁷⁹⁷

953. The HPB assigned numerical designations to differentiate between the gravity of various recalls. A "Class 1" recall was defined as a situation in which there was a "reasonable possibility" that the use of a product would cause serious adverse health consequences or death. "Class 2" was designated where use of the product might cause temporary adverse health consequences or where the chance that the product would have serious adverse health consequences was remote. A "Class 3" situation was designated where the product was not likely to cause any adverse health consequences.¹⁷⁹⁸

954. The BoB required a recalling party to inform the HPB of the identity of the product recalled, quantity of the product produced, quantity of product distributed up until time of the recall, area distribution, quantity of recalled product in its possession, as well as the reason for initiating the recall.¹⁷⁹⁹

¹⁷⁹⁶ Ex. 997, Vol. 243, Tab 1, p. 109236 (May 14, 1984, Letter to All Recipients of Information Letters Re Product Recall Procedures from A.B. Morrison).

¹⁷⁹⁷ *Ibid.*, p. 109240.

¹⁷⁹⁸ *Ibid.*, p. 109243-109244.

¹⁷⁹⁹ *Ibid.*

955. The Assistant Deputy Minister of Health was to decide if a public recall announcement was mandatory and whether the HPB would issue a recall warning to the public.¹⁸⁰⁰ The party recalling the product was to convey to affected parties or the general public: that the product in question was subject to a recall; that further distribution or use of any remaining product should cease immediately; and that the 'direct account' should notify its 'accounts' in receipt of the product about the recall and instructions on what to do with the recalled stock.¹⁸⁰¹ The HPB stated that recall information could be communicated by telephone, telex, telegram, or special delivery letters. Notices sent orally were to be confirmed in writing.¹⁸⁰²

956. There was regular communication between the BoB, the fractionators and the CRCS about biologicals and concentrates. The HPB and the BoB were involved in monitoring any product withdrawals, recalls, or the removals of concentrates due to concerns about safety. Moreover, the BoB had the power to step in at any point if it appeared that a recall or withdrawal was not being carried out in a satisfactory manner.¹⁸⁰³

¹⁸⁰⁰ *Ibid*, p. 109248.

¹⁸⁰¹ *Ibid*, pp. 109251-109252.

¹⁸⁰² *Ibid*, p. 109252.

¹⁸⁰³ *Evidence of Dr. Furesz, BoB Panel*, pp. 42939 and 42941.

NOTE: For example, in January 1985 the CRCS was notified that certain concentrates contained plasma from an Irwin Memorial blood bank donor who had subsequently developed AIDS. By the time the CRCS received this notification in January 1985, the lots were outdated and there were no vials of this product traceable by the centres. The CRCS informed the BoB that no recall would be issued unless so ordered by the BoB. The BoB did not order a recall.

Evidence of Dr. Davey, former Assistant National Director BTS, pp. 27038-27039.

e) **Formalized Product Recall Protocol**

957. In March, 1984, Dr. Naylor wrote to Dr. Herst regarding her proposal for a uniform recall document:

Your suggestions to ensure uniformity of information transmitted during recalls is very valid and will be adopted.

In analyzing the time required to effect product recall last August and September, it is apparent that the link between Hospital Blood Banks, treating physicians and users is where unacceptable delays occur.

The optimum solution in terms of time savings and costs incurred would be the mechanism by which information is communicated directly from CRC BTS centres to hospitals, treating physicians and users simultaneously with additional communication via the CHS to provide redundancy. Such a method is currently outside the jurisdiction of the BTS.¹⁸⁰⁴

Dr. Naylor further noted that the CRCS was experiencing great difficulty obtaining information on product utilization by hemophiliac patients in Canada.¹⁸⁰⁵

958. Concerns about breakdown in communications between hospitals, treating physicians and users were discussed at the March 1984 Medical Directors' Committee meeting. Dr. Naylor recommended that the CRCS work with the CHS and its provincial chapters, to develop an effective 'grass roots network' to expedite product recall:

Even though these links in the recall chain are outside CRC BTS jurisdiction, if communication is not effective at this level, this will ultimately reflect on the NBTS.¹⁸⁰⁶

¹⁸⁰⁴ Ex. 625, Vol. 22, Tab 8, p. 75939 (March 21, 1984, Letter to Dr. Herst from Dr. Naylor).

¹⁸⁰⁵ Ibid, p. 75940.

¹⁸⁰⁶ Ex. 625, Vol. 22, Tab 21, p. 65991 (Medical Directors' Meeting, March 29-30, 1984, Position Paper. Agenda Item No. 21).

959. In April, 1984, the Blood Components Working Group agreed that a uniform message should be received by users across the country. Editing and editorializing by BTS Centres, hemophilia treatment centres, hospitals, or the CHS could be minimized if the National CRCS issued information in a form suitable for ultimate distribution to patients.¹⁸⁰⁷ One of the Committee's members, Dr. Freedman, a haematologist from St. Michael's Hospital, proposed that hospital blood banks should receive information on recalls before the lay CHS executive and individual users. At the conclusion of the meeting it remained to be determined whether hospital blood banks or the CRCS would be responsible for communicating with the hemophilia treatment centres and treating physicians. Who would communicate with the outpatient users was undecided; however, it was recognized that only in extraordinary circumstances would the local CRCS centre be aware of the identity of the individual patients. It was determined that this was an inappropriate role for the CRCS.¹⁸⁰⁸

960. The blood product services at the CRCS undertook to draft a formal protocol document on recall proceedings with input from the hemophilia treatment community.¹⁸⁰⁹ The CRCS adopted the HPB designation of "Class 1, 2 and 3" recalls and "hazards".¹⁸¹⁰

961. Regardless of whether an action was termed a "return", a "recall" or a "withdrawal", it was always treated seriously by Medical Directors. Centre Directors who were questioned on this issue testified that they treated return and replacement notices as seriously as recall notices.¹⁸¹¹ Dr. Turner testified that when the Centre heard that something was to be

¹⁸⁰⁷ Ex. 757, Vol. 163, Tab 5, p. 39384 (April 27, 1984 Minutes of Blood Components Working Group Meeting).

¹⁸⁰⁸ Ibid, p. 39384.

¹⁸⁰⁹ Ex. 631, Vol. 28, Tab 22 (January 2, 1985, Memorandum to Dr. Blajchman from T. Walker).

¹⁸¹⁰ See Health Protection Branch recall protocol portion in this section at page 486.

¹⁸¹¹ Evidence of Dr. Aleport, Regina Centre Medical Director, pp. 8752-8753; and Evidence of Dr. Huntsman St. John's Centre Medical Director, p. 14006.

withdrawn they would take action on it "right away".¹⁸¹² This was echoed by both Drs. Huntsman and Aleport. As Dr. Buskard testified, the sense of urgency associated with the term "recall" meant that product was withdrawn with no guarantee of replacement, whereas "replacement" referred to returns with product available.¹⁸¹³

962. At the March, 1985 meeting of the Ontario MSAC, Dr. Naylor distributed the draft product recall protocol.¹⁸¹⁴ The draft recall protocol was reviewed by the hemophilia treating physicians at the National MSAC meeting in April of 1985. Dr. Card requested that treating physicians with comments on the protocol contact Dr. Naylor directly.¹⁸¹⁵

963. Over the course of the next year, the CRCS, hemophilia treaters, fractionators and other parties to the blood system provided their input into the draft of the product recall protocol. On May 28, 1986, a written copy of the recall procedure was distributed. The distribution of this formal procedure for product recall was 'new' only insofar as the CRCS was providing a written reminder to all parties in the blood system of their obligations in times of recall. The national protocol was drafted by the CRCS in order to assist other parties in the blood system and provide a reference for these parties. The draft protocol simply formalized the existing CRCS recall procedures.

¹⁸¹² *Evidence of Dr. Turner, Edmonton Centre Medical Director, p. 7624.*

¹⁸¹³ *Evidence of Dr. Noel Buskard, Clinical Professor of Medicine, UBC, pp. 5712.*

¹⁸¹⁴ *Ex. 761, Vol. 167, Tab 21, p. 58 (March 23, 1985 Minutes of CHS Ontario Chapter MSAC).*

¹⁸¹⁵ *Ex. 761, Vol 167, Tab 53, p. 157 (April 19, 1985, Minutes of Meeting of MSAC).*

2) The Withdrawal and Return of Non-Heat-Treated Concentrates

964. As discussed in the heat-treatment section, on November 16, 1984 the BoB issued a recommendation regarding the utilization of heat-treated AHF products.¹⁸¹⁶ In response to this recommendation, the CRCS endeavoured to secure a supply of heat-treated concentrate. At this time, neither the BoB nor the CRCS withdrew or recalled non-heat-treated concentrate. In hindsight, that decision has been criticized for putting hemophiliacs at risk for acquiring AIDS. However, a complete withdrawal of non-heat-treated concentrate was unthinkable having regard to the availability of heat-treated product.

965. As Dr. Boucher testified:

The reason was that they may not have any Factor VIII to use at all. So the decision was that if you have Factor VIII available, because I knew that there was probably - could be up to a six-month delay in getting something through the process - my question was, do you leave that product on the market to use, or do you simply take it off? Certainly, the indication was is (sic) that hemophilia patients would prefer to have the product.¹⁸¹⁷

a) Shortages and the Use of Concentrate

966. As concentrates were viewed as a necessity in the medical care of hemophiliacs, the concept of withdrawing or recalling all non-heat-treated lots and returning hemophiliacs to the use of cryoprecipitate pending the arrival of heat-treated concentrates was unthinkable.¹⁸¹⁸ Throughout 1984, hemophiliacs, through the CHS and its MSAC, had been vocal about shortages and had lobbied for the CRCS to maintain a stable supply of concentrates.¹⁸¹⁹ There had been shortages over the prior year which had led to cancellations of surgery and limited the

¹⁸¹⁶ Ex. 759, Vol. 165, Tab 7 (November 5, 1984 AIDS Update).

¹⁸¹⁷ Evidence Dr. Wark Boucher, BoB Panel, p. 43099.

¹⁸¹⁸ See the Section entitled CRCS Relationship with Hemophiliacs and Hemophilia Treeters Section E.

¹⁸¹⁹ See Section entitled Heat-Treatment.

distribution of supplies of concentrate to hemophiliacs on home-care.¹⁸²⁰ Shortages had occasionally resulted in a return to cryoprecipitate use, which most hemophiliacs found unacceptable.¹⁸²¹

967. Dr. Hughes-Jones, a Cambridge physician stated in his article:

With the wisdom of hindsight, we now know that the decision of most Haemophilia Centres to continue the use of factor VIII concentrates during 1983-1984 was wrong even though most haemophiliacs had probably been infected prior to that period. The reason for the continued use of concentrates was simple, namely, that there was a general consensus at that time that the benefits obtained from factor VIII concentrate therapy **greatly** exceeded any harm that might ensue.¹⁸²² (Emphasis Original)

968. Some individuals believed in the "dilution theory" at this time. Accordingly, there was a concern that an infected dose of cryoprecipitate might pose a greater danger in terms of transmission of a virus to hemophiliacs than the presence of viral particles in lyophilized concentrates diluted in massive amounts of plasma.¹⁸²³ In a December, 1984 paper concerning Factor VIII product use, Bill Mindell wrote:

¹⁸²⁰ As discussed *infra*.

¹⁸²¹ Ex. 758, Vol. 164, Tab 9, p. 50 (Report to the Blood Resources Committee - CHS dated September 11, 1984);

Ex. 758, Vol. 164, Tab 11, p. 55 (Memorandum to Drs. Perrault and Davey from Dr. Naylor re Summary of An Informal Meeting Held With Representatives of The Canadian Hemophilia Society on August 28th, 1984 dated September 13, 1984);

Ex. 758, Vol. 164, Tab 24, p. 95 (Notes on a Meeting re Factor VIII Concentrate Shortages in Canada dated October 11, 1984);

Ex. 758, Vol. 164, Tab 29, p. 121 (Letter to Dr. Card from Dr. Growe dated October 19, 1984); and

Ex. 758, Vol. 164, Tab 30, p. 122 (Summary of a Meeting Between Canadian Hemophilia Society (CHS) and CRC National BTS Representatives dated October 19, 1984).

¹⁸²² Ex. 743, Tab 34, p. 2 (Risk Assessment and the Use of Factor VIII Concentrates during 1983-1985, N.C. Hughes-Jones).

¹⁸²³ Evidence of William Mindell, CHS Member (Ontario Chapter), pp. 32252-32255.

While the former [concentrates] appears to be a much more broad risk because of the numbers of donors involved (and some of the sources of plasma), it is now known that the lyophilization process itself is at least somewhat protective in decreasing retrovirus titres.¹⁸²⁴

969. In the fall of 1984 and into 1985, it was also uncertain as to whether heat-treatment itself would be completely effective in reducing the risk of AIDS in hemophiliacs. It was hoped that heat-treated concentrates would reduce the risk of transmitting the HTLV-III virus, however, there were a number of parties who had serious misgivings about the process.¹⁸²⁵ Bill Mindell testified:

...And myself, and others, had two serious misgivings about heat-treatment. It wasn't proven at that time, with respect to HIV attenuation. There were no in vivo studies. Everything was a laboratory study, in vitro. The second one was that these concentrates, and the problem with heat-treatment in the first place was that it had never really been effective in stopping hepatitis.¹⁸²⁶

b) CRCS Action on Withdrawal of Non-Heat-Treated Concentrates

970. Commencing June, 1985, the BTS and local centres replaced all non-heat-treated concentrates in both local centre stocks, hospital blood banks, and hemophilia care supplies with heat-treated concentrate. At the time of this withdrawal and replacement, the CRCS had already incorporated recommendations made over 1983 and 1984 as to how to better alert consumers on recalls.¹⁸²⁷

¹⁸²⁴ Ex. 759, Vol. 165, Tab 36, p. 110 (December 4, 1984 Letter from Bill Mindell to Linda Laxdal, Mr. Rudd, Ken Poyser and Dr. Card).

¹⁸²⁵ Evidence of Dr. Schroeder, Winnipeg Centre Medical Director, pp. 10009-10010; and

Evidence of Dr. Turc, former Edmonton Centre Medical Director, pp. 7519-7520.

¹⁸²⁶ Evidence of William Mindell, CHS Member (Ontario Chapter), p. 32249.

¹⁸²⁷ One important suggestion was made by Dr. Herst who proposed that a universal letter be provided by national office to hospital blood banks and hemophilia treatment centres.

Ex. 755, Vol. 161, Tab 65, p. 168 (November 15, 1983, Memorandum to Dr. Naylor from Dr. Herst re: Communication About Fractionation Recall).

971. On June 20, 1985 the Medical Directors and Technical Supervisors of the CRCS were updated on the conversion to heat-treated concentrate. This memo reviewed the recall and return procedures to be followed. Effective July 1, 1985, BTS centres were to issue only heat-treated concentrates; all non-heat-treated factor VIII and IX product was to be withdrawn from hospital and home inventories. Returns to BTS centres were to be completed by July 31, 1985. Directions for recording the returns was provided.¹⁸²⁸ A copy of the memo was carbon-copied to Dr. Card of the CHS and to the Hemophilia Treatment Centre Directors with attachments. In addition, attached to the memo were the concentrate return forms. The memo outlined the reasons for the return as well as the status of the supply of concentrates to September 1985.¹⁸²⁹

972. On June 28, 1985 the national CRCS issued a press release announcing the exclusive use of heat-treated concentrates. This press release advised that heat-treated concentrates had a possible reduced rate of HIV transmissibility and were thought to be safer:¹⁸³⁰

All remaining stocks of non-heat-treated products are being withdrawn from use. Hemophilia patients and hemophilia treatment centres that now have untreated products may return them in exchange for heat-treated Factor VIII or IX.¹⁸³¹

973. At the local level, the BTS communicated directly with hospital blood banks and with hemophilia treating physicians. It forwarded them copies of the CRCS national notice and its locally-drafted notices advising them to return all non-heat-treated concentrates. Aware of

A further suggestion, made by Dr. Card, was that Hemophilia Treatment Centre Directors be notified by National Office of returns or withdrawals in order that they could begin to trace product. Thus the treaters would not have to rely solely on the hospital blood bank to provide information to the centres.

Ex. 761, Vol. 167, Tab 2 (February 27, 1985, Letter to Dr. Naylor from Dr. R. Card).

¹⁸²⁸ *Ibid, Tab 15.*

¹⁸²⁹ *Ex. 636, Vol. 33, Tab 15 (June 20, 1985, Memorandum to Medical Directors, Technical Supervisor from Dr. Naylor Re: Update on Conversion to Heat-Treated VIII and IX Concentrate).*

¹⁸³⁰ *Ex. 636, Vol. 33, Tab 23 (June 28, 1985 Press release "Red Cross Increases Safety of its Blood Products").*

¹⁸³¹ *Ibid, Tab 23.*

previous shortcomings in the communication system between the hospitals, treaters and the individual patients, the national office issued a nation-wide press release on June 28, 1985 to all national news wires for immediate release advising hemophiliacs of the switch to heat-treated concentrate and the withdrawal and exchange of non-heat-treated product.¹⁸³² Moreover, this release was also copied to all Commissioners and the Director General of each Division in addition to the individual Medical Directors.¹⁸³³ Finally, hemophiliacs were further advised of the switch in *Hemophilia Today*, the national CHS Bulletin.¹⁸³⁴

974. The particulars of recalls of non-heat-treated product at the local level were canvassed with some Medical Directors. All centres underwent the same general procedure to recall the heat-treated product, however the following outlines the specific procedures in some of the centres discussed in evidence.¹⁸³⁵

i) Vancouver Centre

975. On June 26, 1985 Amin Adatia, Technical Director of Vancouver Centre, notified the Chief Medical Technologists of the area blood banks, that BTS was "recalling all non-heat-treated Factor VIII and IX" concentrates. The blood bank medical technologists were instructed to record the amount of concentrate returned to the Centre for credit. The hemophilia patients were contacted by Lois Lidner of the Hemophilia Assessment Clinic.¹⁸³⁶ Follow-up on the returns was conducted on August 1, 1985 when Mr. Adatia wrote to Marilyn Stark and June Humphreys to confirm whether there were any hospitals or hemophiliacs who had not returned.

¹⁸³² Ex. 636, Vol. 33, Tab 33 (June 28, 1985, Press Release entitled "Red Cross Increases Safety of Its Blood Products").

¹⁸³³ Ex. 763, Vol. 169, Tab 19 (June 28, 1985 Telex from Eva Bart to All Divisions, Medical Directors re: Press Release).

¹⁸³⁴ Ex. 28, Vol. 11, p. 2184 (April, 1985, *Hemophilia Today*, Vol. 25, No. 3).

¹⁸³⁵ Note that evidence on recalls and withdrawals was not uniformly canvassed from all centres during the Inquiry.

¹⁸³⁶ Ex. 111, Vol. 47, Tab 23 (June 26, 1985 Memorandum to Chief Medical Technologists, Blood Bank, from Amin Adatia).

non-heat-treated concentrates.¹⁸³⁷ The National office received detailed information from Vancouver which summarized the returns of non-treated concentrates, including hospitals, number of vials, unit vial numbers and lot numbers.¹⁸³⁸

976. On September 30, 1985, thirty-eight vials of non-heat-treated concentrates were returned to National office from Vancouver Centre. These vials had been returned by patients who were on holiday over July and August. Information about particular patients was in the hands of the hospital blood bank, which issued the concentrates to the hemophiliacs in question, and their treating physicians. The CRCS did everything in its power in order to facilitate the return of untreated concentrate, including follow-up in August.¹⁸³⁹

977. Dr. Buskard, of Vancouver Centre, testified that the Hemophilia Assessment Clinic was usually responsible for contacting patients directly.¹⁸⁴⁰ Dr. Buskard testified that delays in notifying patients occurred when patients were out of the area for summer holidays. The recall information was promptly relayed to hospital blood banks and treating physicians by the CRCS. If the hospital was not successful in contacting the patient, the CRCS could do little else as it did not have access to patient lists. The CRCS could not determine which patients were on homecare or whether they not they had indeed been contacted.¹⁸⁴¹

¹⁸³⁷ Ex. 111, Vol. 47, Tab 31 (August 1, 1985 Memorandum from Amin Adatia to Marilyn Stark and June Humphreys re: Conversion to heat-treated Factors VIII and IX).

¹⁸³⁸ Ex. 111, Vol. 47, Tab 32, pp. 53045-53050 (Memorandum August 9, 1985 to Dr. Naylor from Amin Adatia).

¹⁸³⁹ Ex. 111, Vol. 47, Tab 40 (Memorandum dated September 30, 1985 to Craig Anhorn from Amin Adatia):

Evidence of Dr. Buskard, Clinical Professor of Medicine, UBC, pp. 5585 - 5586.

¹⁸⁴⁰ *Evidence of Dr. Buskard, Vancouver Centre, p. 5580.*

¹⁸⁴¹ *Ibid, pp. 5585-5586.*

ii) St. John's Centre

978. In a memo of May 30, 1985 Dr. Naylor requested that all Medical Directors contact the Hemophilia Treatment Centres to ascertain the surgical load that could be anticipated during the period of July to September.¹⁸⁴² The memo reminded them that there would be an increase in the demand for Factor VIII after July 1 when hemophiliacs on home-care would "require product to replenish their stocks".¹⁸⁴³ On June 13, 1985, Joy Bartlett of the Hemophilia Treatment Centre wrote to Tom Peddle of the St. John's BTS Centre, in response to his request for an estimate of concentrate usage over July to September. This memo demonstrated that the BTS and local Hemophilia Treatment Centres were co-operating in the conversion to heat-treated concentrates.

979. The Hemophilia Treatment Centre at Janeway Hospital was copied with the memo instructing Centres that the withdrawal of heat-treated concentrates was to occur over the month of July with returns completed by July 31. The withdrawal and replacement of non-heat-treated concentrates was undertaken by the Hemophilia Treatment Nurse Coordinator, who directly contacted the hemophiliacs. The recall of non-heat-treated concentrates was accomplished by direct phone contact, followed by letters.¹⁸⁴⁴

980. Newfoundland BTS staff followed up on their previous direction to the Hemophilia Treatment Centres and hospitals. They contacted Joy Bartlett by phone concerning the returns on July 5, 1985.¹⁸⁴⁵ Four Newfoundland hospitals were also phoned in connection with the return of non-heat-treated concentrates.¹⁸⁴⁶

¹⁸⁴² Ex. 762, Vol. 168, Tab 45, p. 80 (May 30, 1985, Memorandum to Medical Director, Technical Supervisor from Dr. Naylor Re: Update on Conversion to Heat-Treated Factors VIII and IX Concentrates).

¹⁸⁴³ Ibid, p. 80.

¹⁸⁴⁴ Evidence of Dr. Huntsman, St. John's Centre Medical Director, pp. 14006-14008.

¹⁸⁴⁵ Ex. 333, Vol. 96, Part II, Tab 1, p. 1 (Factor VIII Handwritten Recall Chart).

¹⁸⁴⁶ Ibid, p. 1.

iii) Saint John Centre

981. While New Brunswick did not have a Hemophilia Treatment Comprehensive Care Clinic, Dr. MacKay, Medical Director of Saint John Centre was in contact with the physicians who were responsible for primary hemophilia treatment care in the province. On June 24, 1985, Dr. MacKay wrote to Dr. Pond in Moncton and Dr. Rubin in Saint John, to inform them that commencing July 1, 1985, the Centre would distribute only heat-treated concentrates.¹⁸⁴⁷ Dr. MacKay testified that he was not aware of any other physicians in the province treating hemophiliacs.¹⁸⁴⁸

982. The Saint John Centre staff also contacted all hospital blood banks and requested that non-heat-treated concentrate be returned to the BTS Centre.¹⁸⁴⁹ Returned non-heat-treated concentrate to the Centres was forwarded to National Office during the first week of August.¹⁸⁵⁰

iv) Winnipeg Centre

983. The Winnipeg BTS Centre and the local hemophilia treatment physicians clearly cooperated in the conversion to heat-treated concentrates.¹⁸⁵¹ CRCS Winnipeg Centre

¹⁸⁴⁷ Ex. 279, Vol. 85, Part I, Tab 4, pp. 69 - 70 (June 24, 1985 Letters from Dr. Makay to Dr. Pond and Dr. Rubin).

¹⁸⁴⁸ Evidence of Dr. MacKay, Saint John Centre Medical Director, pp. 11867-11868.

¹⁸⁴⁹ Evidence of Mary Lynne Roy, Laboratory Manager of Saint John Centre, pp. 11868-11870.

¹⁸⁵⁰ Ibid, p. 11869.

¹⁸⁵¹ Ex. 219, Vol. 74, Part I, pp. 115 - 116 (May 2, 1985, Letter to Dr. Schroeder from Norris Schwetz and Dr. Kobrinsky);

Ex. 219, Vol. 74, Part I, p. 117 (May 3, 1985, Memorandum to Dr. Rayner et al. from Dr. Schroeder Re: Heat-Treated Concentrate); and

Ex. 219, Vol. 74, Part I, p. 118 (April 25, 1985, Letter to Dr. Naylor from Dr. Card Re: Heat-Treated Concentrates, Implementation).

facilitated the return of non-heat-treated concentrates by telephoning the hospitals to request the return of concentrates. The hemophiliac patients were then contacted directly by the treaters.¹⁸⁵² Upon the return of untreated concentrates, the inventory was reconciled and the untreated products were physically segregated.¹⁸⁵³ In accordance with National office directions, returns were made on August 7 and again on August 17.¹⁸⁵⁴

984. Manitoba was a unique province as Winnipeg Centre had a centralized "cross-match" system. Therefore, the Centre knew the location of Factor VIII concentrates. Staff at this Winnipeg Centre telephoned each hospital and reviewed all vials in stock to ensure that all product was returned and replaced with heat-treated concentrates.¹⁸⁵⁵

v) Saskatoon Centre

985. On June 26, 1985, Dr. McSheffrey notified all hospital pharmacies and blood banks that as of July 1, 1985 only heat-treated concentrate would be supplied. All stocks of non-treated Factor IX were to be returned to the CRCS for credit:

We have been asked to complete this by the end of July. To facilitate this conversion please reorder your normal stocks early in July... Please return to us any unused non heat-treated Factor IX by the end of July.

We are contacting hemophiliacs on home therapy to return their non-heat-treated Factor IX concentrates to you for replacement. If you know of any we missed

¹⁸⁵² *Evidence of Dr. Schroeder, Winnipeg Centre Medical Director, p. 9977.*

¹⁸⁵³ *Ibid, pp. 9978-9979.*

¹⁸⁵⁴ *Evidence of Dr. Schroeder, Winnipeg Centre Medical Director, pp. 9979-9980; and*

Ex. 220, Vol. 74, Part II, pp. 257-267 (Withdrawal Charts, Winnipeg Centre Non-Heat-Treated Concentrate).

¹⁸⁵⁵ *Evidence of Dr. Schroeder, Winnipeg Centre Medical Director, p. 10058.*

please inform them. I enclose a list of hemophiliacs we are sending letters to.
Please treat this information as strictly confidential.¹⁸⁵⁶

This memo was carbon copied to Dr. Card as well as Dr. Sheridan and Diane Duforur of Patient Education with University Hospital.¹⁸⁵⁷

986. Dr. McSheffrey was in a different position than other Centre Medical Directors, as he was also a part-time hemophilia treater. Dr. McSheffrey worked closely with Dr. Robert Card, the Chair of MSAC, in the treatment of hemophiliacs at the Saskatoon Comprehensive Care Clinic from 1975 to 1987.¹⁸⁵⁸ On June 26, 1985 Dr. McSheffrey sent "Dear Hemophiliac" letters to known hemophiliacs advising that the centre was converting to heat-treated concentrate use. Patients were advised that if they had unused stock of non-heat-treated IX they were to return it to the hospital where they normally picked up their concentrates.¹⁸⁵⁹ Due to Dr. McSheffrey's unique role, he was in a position to identify many hemophiliacs covered by the comprehensive care services in Saskatchewan. Thus, his Centre could contact many hemophiliacs directly. This was not possible in other CRCS centres as patient names were not available, nor was there a physician/patient relationship between BTS staff centres and hemophiliacs.

vi) Toronto Centre

987. In accordance with the MSAC recommendations, as well as earlier suggestions, the May 30 and June 20, 1985 National memos outlining the withdrawal of non-heat-treated concentrate were copied to Hemophilia Treatment Centre Directors. Forms to report return of

¹⁸⁵⁶ Ex. 188, Vol. 70, Tab 5, p. 48 (June 26, 1985, Letter to All Hospital Pharmacies and Blood Banks Where We Ship Factor IX).

¹⁸⁵⁷ Ibid, p. 48.

¹⁸⁵⁸ Evidence of Dr. McSheffrey, Saskatoon Centre Medical Director, pp. 8323-8326.

¹⁸⁵⁹ Ex. 188, Vol. 70, Tab 5, p. 49 (June 26, 1985, Letter to Hemophiliac Patient from Dr. McSheffrey).

concentrates were attached to these memos.¹⁸⁶⁰ At Toronto Centre, Deputy Medical Director Dr. Herst, took other actions to ensure that any hemophiliacs not contacted by blood banks would be notified through the auspices of the CHS. On June 28, 1985, Dr. Herst wrote to Robert O'Neill, Director of the Ontario Chapter of the CHS:

As you know, all the coagulation factor concentrates issued after July 1st will be heat-treated. All the Canadian Red Cross BTS Centres have been requested to return any non-heat treated preparations to national BTS.

Toronto Centre has sent the enclosed notice to all the Central Ontario hospitals to which coagulation factors are issued. It would assist the return process for the coagulation concentrates if you could disseminate this message to your membership in some appropriate way.¹⁸⁶¹

988. Dr. Herst also sent memos to hospitals which received concentrates.

Please return any non-heat treated coagulation factor preparations you still have in stock after July 1st.

Please request the hemophiliac patients who maintain a home inventory for home infusion to return to you any non-heat treated preparations they still have.¹⁸⁶²

989. Ontario hemophiliacs received notice through the July/September, 1985 issue of *Hemophilia Ontario*. The front page of *Hemophilia Ontario* announced: "Heat-Treated Products Are Here!"¹⁸⁶³

¹⁸⁶⁰ Ex. 513, Vol. 115, Part II, p. 487 (May 30, 1985, Memorandum to Medical Director/Technical Supervisor from Dr. Naylor Re: Update on Conversion to Heat-Treated Factors VIII and IX); and

Ex. 513, Vol. 115, Part II, p. 489 (June 20, 1985, Memo to Medical Director from Dr. Naylor Re: Update on Conversion to Heat-Treated Factors VIII and IX).

¹⁸⁶¹ Ex. 513, Vol. 115, Part II, p. 499 (June 28, 1985, Letter to Robert O'Neill from Dr. Herst).

¹⁸⁶² Ex. 513, Vol. 115, Part II, p. 500 (June 28, 1985, Memorandum to Hospitals from Dr. Herst).

¹⁸⁶³ Ex. 763, Vol. 169, Tab 21 (July-September, 1985 issue of *Hemophilia Ontario*).

990. Each of the Toronto Hemophilia Treatment Centres had its own internal procedures for contacting patients to facilitate return of unused concentrates.¹⁸⁶⁴ The CRCS Toronto Centre did not have access to information about individual patients nor did the Centre have knowledge of which patients received which concentrates.¹⁸⁶⁵

vii) Ottawa Centre

991. The Ottawa Centre issued a notice to blood bank directors, charge technologists and haematologists on June 4, 1985 providing an update on the conversion to heat-treated factor concentrates.¹⁸⁶⁶ The bulletin stated that full conversion to heat-treated products would occur after July 1, 1985. Dr. Decary's notice used language identical to that in the May 30, 1985 memo drafted by Dr. Naylor on conversion to heat-treated concentrates.¹⁸⁶⁷

992. On June 24, 1985, Dr. Decary again wrote to blood bank directors, haematologists and charge technologists at blood banks to update them on "the action to be taken during the next month". All non-heat-treated Factor VIII and IX concentrate was to be withdrawn from hospital inventories and hemophilia home inventories and returned to Ottawa Centre by July 31, 1985.¹⁸⁶⁸

¹⁸⁶⁴ Dr. Teitel of St. Michael's Hospital Comprehensive Hemophilia Care Program testified that hemophilia patients were called by Anne Harrington, Nurse Co-ordinator of the program. Any problems with contacting hemophiliacs occurred between treating physicians, comprehensive care clinics and the individual patients.

Evidence of Dr. Teitel, Medical Director of Hemophilia Ontario, p. 33921.

¹⁸⁶⁵ Evidence of Dr. Teitel, Medical Director of Hemophilia Ontario, pp. 33918-33919.

¹⁸⁶⁶ Ex. 603, Vol. 154, p. 94 (June 4, 1985, Memorandum from Dr. Decary re: Update on Conversion to Heat-Treated Factors VIII and IX Concentrate).

¹⁸⁶⁷ Evidence of Dr. Rock, former Ottawa Centre Medical Director, pp. 23989-23891.

¹⁸⁶⁸ Ex. 603, Vol. 154, p. 96 (June 24, 1985, Memorandum from Dr. Decary on Update to Conversion to Heat-Treated Factor VIII and IX Concentrate).

viii) Hamilton Centre

993. The return of non-treated concentrates was undertaken in the same manner as other local centres. Staff at Hamilton Centre communicated with hemophilia treaters in the Hamilton area. On May 14, 1985, a memo was sent to Blood Bank Directors and copied to Drs. Pai, Walker and Ali, area hemophilia treaters, summarizing the status of conversion to heat-treated concentrates. In addition, Dr. Blajchman provided the treaters with copies of the new package inserts for Armour's heat-treated concentrates.¹⁸⁶⁹

994. Hamilton Centre staff consulted with hemophiliac treaters to ascertain the number of patients requiring heat-treated concentrate during the conversion period.¹⁸⁷⁰ On July 2, 1985, Dr. Blajchman issued memos to the blood bank directors, chief technologists in all hospitals, and Drs. Pai and Walker requesting that all non-heat-treated Factor VIII and IX concentrates be withdrawn from hospital and hemophiliac home inventories. Returns were to be completed by July 31. Dr. Blajchman concluded:

Your co-operation in this matter would be gratefully appreciated to ensure a smooth transition to heat-treated products.¹⁸⁷¹

¹⁸⁶⁹ Ex. 492, Vol. 119, Part I, p. 71 (May 14, 1985, Memorandum to Blood Bank Directors and Chief Technologists from Dr. Blajchman).

¹⁸⁷⁰ Ibid, p. 79 (May 30, 1985, Memorandum to Medical Directors from Dr. Naylor Re: Update on Conversion to Heat-Treated Factors VIII and IX Concentrates);

Ibid, p. 81 (Undated, Memo to Dr. Naylor from Christina Spiak Re: Heat-Treated Factor VIII Concentrate); and

Ibid, p. 82 (June 20, 1985, Memo to Medical Directors/ Technical Supervisor from Dr. Naylor Re: Update on Conversion to Heat-Treated Factors VIII and IX Concentrate).

¹⁸⁷¹ Ibid, p. 95 (July 2, 1985, Memorandum to Blood Bank Directors et al. from Dr. Blajchman)

ix) London Centre

995. London Centre staff reported an excellent working relationship with the local hemophilia treatment program. There was extensive and ongoing communication between the hemophilia programs and the Centre concerning the conversion to heat-treated concentrates.¹⁸⁷²

The hemophilia treaters in the area, in cooperation with the London CRCS, developed a unique numbering system for factor concentrates, which allowed the hemophilia program to identify whether particular vials had been used by a hemophiliac. It was "an excellent method of indicating to the hemophiliac, our intent of ensuring complete compliance with our instructions".¹⁸⁷³ This cooperative venture enabled both the BTS and hemophilia program to successfully monitor hemophiliacs on home care. The program ensured that there was a smooth

¹⁸⁷² Ex. 506, Vol. 120, Part I, p. 141 (April 17, 1985, Memorandum to Dr. Barr from Dr. Inwood Re: Distribution of Heat-Treated Coagulation Factor Products);

Ibid, p. 142 (April 25, 1985, Letter to Dr. Naylor from Dr. Card Re: Heat-Treated Factor Concentrates, Implementation Period);

Ibid, p. 143 (April 29, 1985, Memo to BTS Centre Medical Directors from Dr. Naylor Re: Implementation and Distribution of Heat-Treated Coagulation Factor Products);

Ibid, p. 144 (May 6, 1985, Letter to Dr. Inwood from Dr. Barr Re: Distribution of Heat-Treated Coagulation Factor Products);

Ibid, p. 146 (May 16, 1985, Memo to Dr. Barr from Dr. Inwood Re: Distribution of Heat-Treated Coagulation Factor Products);

Ibid, p. 149 (May 23, 1985, Letter to Dr. Inwood from Dr. Barr Re: Distribution of Heat-Treated Coagulation Factor Products);

Ibid, p. 151 (May 30, 1985, Memo to Medical Directors/ Technical Supervisor from Dr. Naylor Re: Update on Conversion to Heat-Treated Factors VIII and IX Concentrates);

Ibid, p. 153 (June 6, 1985, Memo to Dr. Naylor from Edi Dinel Re: Conversion to Heat-Treated Factor VIII and IX Concentrates); and

Ibid, p. 154 (June 20, 1985, Memo to Medical Director from Dr. Naylor Re: Update on Conversion to Heat-Treated Factors VIII and IX).

¹⁸⁷³ *Ibid*, p. 147 (May 17, 1985, Letter to Dr. Barr from Dr. Inwood).

Dr. Inwood reported that the numbering system utilized by the comprehensive care centre resulted in "an increased accuracy of records".

withdrawal of non-heat-treated concentrates. On June 28, 1985, Jennifer Crump, the Hemophilia Program Nurse reported to the Blood Transfusion Service Directors:

As of July 1, 1985, all hemophiliacs presently receiving concentrated Factor VIII and IX, will be supplied with heat-treated concentrates. All those who are on supervised home infusion programs will be asked to return the unused portion of their current supply to you, to have a 15 ml. red top tube of blood taken and to receive their new supply of heat-treated concentrate.¹⁸⁷⁴

996. On July 4, 1985, Edi Dinell, a technical supervisor from London CRCS sent a memo to the blood bank supervisors. Area hospitals were to return non-heat-treated Factor VIII and IX concentrate to London Centre. Ms. Dinell outlined the procedure for concentrate returns:

1. Please collect all non-heat-treated products from your hospital inventory as well as from the home inventories of the hemophiliacs which you supply.
2. List all of the products you are returning in the appropriate enclosed forms along with their unique numbers.
3. Return all of the non-heat-treated products along with the completed forms to the London Centre before July 26, 1985.¹⁸⁷⁵

997. The local hemophilia treatment centre in the London area also participated in ensuring that non-heat-treated concentrates from hemophiliac home inventories were returned to BTS Centre. In an edition of a *Medical Corner* newsletter directed to local hemophiliacs, Dr. Inwood advised hemophiliacs that:

As of July 1, 1985, we will begin switching over to heat-treated concentrate. Everyone presently using Factor VIII and IX concentrates will be asked to return all unused concentrate to their supplying hospital along with their completed diary sheets. A blood sample will be taken and supply of heat-treated concentrate distributed. It is essential that all hemophiliacs comply with the

¹⁸⁷⁴ Ibid, p. 158 (June 28, 1985 Memorandum from J. Crump Re: Conversion to Heat-treated Factor VIII and IX Concentrates).

¹⁸⁷⁵ Ibid, p. 160 (Memorandum from Edi Dinell Re: Conversion to Heat-treated Factor VIII and IX Concentrates).

instructions they are given in order that a smooth transition can be accomplished by July 31, 1985.¹⁸⁷⁶

¹⁸⁷⁶ Ex. 812, Vol. 182, Part II, Tab 6, p. 15 (Summer, 1985, Medical Corner).

H. LOOKBACK/TRACEBACK FOR AIDS

1) Introduction

998. A traceback is the process of locating and testing all donors of blood or blood component received by a patient who is subsequently found to test positive for a transmissible disease (eg. AIDS) following a blood transfusion. Traceback originates with the hospital or doctor who discovered the patient's positive test status.

999. A lookback is the process of identifying and notifying recipients of any *previous* donations from a donor who has been identified as having a transmissible disease as a result of either routine testing or in the context of a traceback investigation. Lookback originates with a donor who is found to test positive.¹⁸⁷⁷

1000. CRCS Medical Directors conducted lookbacks and tracebacks for AIDS once TAA cases arose in their centres, well before formal national policies were in place and before testing was implemented. Tracebacks for AIDS were an extension of the policy already in place by 1980 to respond to cases of post-transfusion hepatitis B.¹⁸⁷⁸

¹⁸⁷⁷ *Evidence of Dr. Herst, Toronto Centre Medical Director, pp. 21430-21432; and*

Evidence of Dr. Buskard, former Vancouver Centre Medical Director, pp. 5557-5558.

¹⁸⁷⁸ *Evidence of Dr. Schroeder, Winnipeg Centre Medical Director, pp. 9893-9895;*

Evidence of Dr. Davey, former Assistant National Director BTS, pp. 29992-29993;

Evidence of Dr. Guevin, former Montreal Centre Medical Director, p. 15843;

Evidence of Dr. Perrault, former National Director BTS, p. 29684; and

Evidence of Dr. Herst, Toronto Centre Medical Director, pp. 931-932 and 21263.

2) Tracebacks

1001. The first two Canadian adult cases of TAA were reported to the Vancouver CRCS in March and April, 1985. In July, 1985 two additional cases were reported to the CRCS. There was prompt response to all of these cases. The April 1985 case involved only 17 donors. The Vancouver CRCS formulated a procedure and commenced a review of its records and contacted those donors from May 21, 1985 to June 2, 1985. The experience gained in this relatively small traceback formed the foundation for the procedure undertaken to conduct subsequent tracebacks.

1002. For this case and the others reported in July, the Vancouver CRCS drafted an experimental Standard Operating Procedure (hereinafter referred to as "SOP") entitled *Possible Recommended Standard Procedures for Cases of Post-transfusion AIDS Mortality*.¹⁸⁷⁹ This was subsequently informally known as "Operation 300".

1003. Operation 300 encompassed the March and July 1985 cases reported to the Vancouver CRCS and was more onerous and more complicated than the April 1985 case reported because it involved hundreds of donors who resided both in Canada and elsewhere. It was fully instituted by the end of July 1985, once the procedure and funding were in place and a special projects registered nurse was hired. The hospital in which the recipient had been transfused provided the CRCS with the identification numbers associated with the units transfused. The CRCS then manually searched its records for the identity of the implicated donors, notified them and requested them to attend for testing. Any blood derivatives manufactured from subsequent donations made by the implicated donors were immediately recalled and retrieved.¹⁸⁸⁰

¹⁸⁷⁹ Ex. 111, Vol. 47, Tab 19 (Memorandum from Mr. Robinson, Centre Administrator, to Dr. Davey, dated June 20, 1985 forwarding, "Possible Recommended Standard Procedures for Cases of Post-transfusion AIDS Mortality"); and

Ibid, Tab 26 (Post Transfusion AIDS in B.C. Sequence of Events, undated).

¹⁸⁸⁰ *Ibid*, (Memorandum from Mr. Robinson, Centre Administrator, to Dr. Davey, dated June 20, 1985 forwarding, "Possible Recommended Standard Procedures for Cases of Post-transfusion AIDS Mortality").

1004. Operation 300 was terminated on December 31, 1985. In total, 349 donors were involved in the March and July cases reported to the CRCS. Only 49 of the implicated donors were unable to be traced. 83% of those contacted agreed to be tested.¹⁸⁸¹

1005. In August, 1985, a case of TAA was reported to the Ottawa CRCS. Using a modified version of the Vancouver centre SOP, Ottawa conducted its traceback.¹⁸⁸²

1006. The Vancouver and Ottawa centre experiences formed the basis for the September 5, 1985 standardized national policy entitled *Procedure for Reporting Transfusion-Related Reactions*. This policy provided the basis to conduct traceback for cases of post-transfusion AIDS, hepatitis, cytomegalovirus, Epstein-Barr virus, syphilis, and malaria.¹⁸⁸³

3) Lookbacks

1007. After the implementation of testing in November 1985, centres commenced lookbacks of any previous donations made by donors who tested positive. The procedure evolved with the experience of the centres until it was formalized in an SOP distributed on September 16, 1987 and officially implemented.¹⁸⁸⁴ Most centres, however, were conducting

¹⁸⁸¹ Ex. 111, Vol. 47, Tab 61 (Memorandum from Mr. Robinson to Dr. Buskard re: Operation 300 - Final Report, dated January 16, 1986).

¹⁸⁸² Ex. 671, Tab 56 (Article from the Citizen entitled, "Ottawa man contracted AIDS after blood transfusion at Civic", dated October 15, 1985).

¹⁸⁸³ Ex. 111, Vol. 47, Tab 36 (*Procedure for Reporting Transfusion-Related Infections*, dated September 5, 1985).

¹⁸⁸⁴ Ex. 649, CRC Vol. 46, Tab 35 (*Lookback Guidelines*, dated July 6, 1987 and circulated September 16, 1987).

lookbacks before the formal national policy was in place,¹⁸⁸⁵ as was stated in a 1986 memorandum:

¹⁸⁸⁵ *Evidence of Dr. Davey, former Assistant National Director BTS, pp. 29991-29993;*

Dr. Ross was not the Charlottetown Medical Director at the time and could not give evidence as to when lookbacks began in Charlottetown. See Evidence of Dr. Ross, Medical Director of PEI Centre, pp. 13517-13519. Dr. Rock, former Medical Director of the Ottawa Centre was not asked about the issue of lookbacks. Dr. Strong of the Sudbury Centre did not testify and there is no evidence as to when his Centre began lookbacks;

Evidence of Dr. Buskard, former Vancouver Centre Medical Director, p. 5871;

Evidence of Dr. Herst, Toronto Centre Medical Director, pp. 21430-21432;

Ex. 333, Vol. 96, Part II, Tab 2, p. 148 (Summary Report of Lookback Operation, Starting date: November 12, 1985, Completion date: April 1986);

Evidence of Dr. Gorelick, Halifax Centre Medical Director, pp. 12952-12954, 13055;

Ex. 303, Vol. 91, Tab 1, p. 214 (Summary Report of Lookback Operations);

Ex. 164, Vol. 60, Tab 39 (Memo from Dr. Allaire to Dr. Davey re: Lookback of HIV Seropositive Donors in Calgary, dated February 17, 1986);

Evidence of Dr. Schroeder, Winnipeg Centre Medical Director, pp. 9898-9900;

Ex. 220, Vol 74, Part II, p. 73 (Letter from Dr. Rayner to Dr. Fast re Lookback Programmed - Blood Donors with Positive HIV Status, dated November 13, 1987);

Ex. 187, Vol. 69, Tab C, p. 173 (Summary Report of Lookback Operation). [p. 168 First Positive Donation];

Evidence of Dr. MacKay, Saint John Centre Medical Director, pp. 11880-11881;

Ex. 280, Vol. 85, Part II, Tab D, p. 30 (Letter from Dr. Tinning to Dr. Derrick, dated May 22, 1986);

Evidence of Dr. Blajchman, Hamilton Centre Medical Director, pp. 19486-19489;

Evidence of Dr. Turner, Edmonton Centre Medical Director, pp. 7584-7585;

Ex. 147, Vol. 61, Tab 26 (The Red Cross and AIDS Prevention, September 1987);

Ex. 364, Vol. 107, Part 3, Tab D, (Donor Unit Summary Form Lookback);

Evidence of Dr. McSheffrey, Saskatoon Centre Medical Director, pp. 8850-8851;

Ex. 511 (Summary Report of Lookback Operations); and

The evidence is not complete for the Montreal, Ottawa, Sudbury and Charlottetown Centres.

If any donor who has previously donated blood is found to be antibody positive, either as a result of testing a regular donation or because of an investigation into a case of TAA, CRCS does its best to notify the recipients of components or products prepared from earlier donations...¹⁸⁸⁶

4) The Need to Prioritize

1008. The date centres commenced lookbacks was dependent upon staff centre resources and the date upon which a donor was identified as testing positive. Operation 300 clearly demonstrated that lookbacks and tracebacks were enormous undertakings, which required considerable time commitment and the dedication of additional staff. Centre staff, who were already working to capacity, were required to make time for this new and important task, pending funding support from the CBC for additional staff. As discussed previously, CBC approval was required for every additional staff member.¹⁸⁸⁷

1009. Tracebacks were considered top priority because the search was initiated with a known case of AIDS in a recipient whose only risk factor was a blood transfusion. The CRCS centre staff identified implicated donors and immediately disposed of any units associated with them. Priority was then given to traceback-associated lookbacks, followed by lookbacks, as soon as confirmatory testing was available by mid-December, 1985.¹⁸⁸⁸

1010. Despite the apparent discrepancy in the dates between Canada and the U.S., some CRCS centres were conducting lookbacks prior to the American Red Cross national lookback

¹⁸⁸⁶ Ex. 647, CRC Vol. 44, Tab 23 (Memo from Kenneth Mews to File, dated December 5, 1986 re: Recent Coverage of US Blood Banking Industry by the Television Program 20/20).

¹⁸⁸⁷ Evidence of Randy Klotz, CBC Panel, pp. 36839-36841; and
Evidence of Claude Morin, former National Administrator, p. 40010.

¹⁸⁸⁸ Evidence of Dr. Davey, former Assistant National Director BTS, pp. 29993-29994; and
Evidence of Dr. Herst, Toronto Centre Medical Director, p. 21432.

policy, which was announced on June 18, 1986.¹⁸⁸⁹ The difference between the American and Canadian situations was commented upon by Dr. Davey during testimony:

...Well, one was aware of that and this was the Canadian position taken. And we rather took the attitude that in trace-back first and look-back subsequently, that this would be undertaken locally, according to procedures developed for local conditions and that as experience accumulated, it would be possible to develop national guidelines for this, based on the actual experience and problems encountered.

Now, the U.S. took the other direction and said, "We will issue our procedures and guidelines, we'll then see how they apply," and, you know, either maintain them or change them.

But I would say we were, particularly in trace-back which was already going on at this time of course, we were, as it were, building from the field towards a national system.

Whereas, the U.S. started with a national system and tested in the field. It is a different type of approach to this question.¹⁸⁹⁰

5) **CBC's Position Regarding the Need for CRCS Computerization**

1011. While CRCS record-keeping was complete and accurate, it was not computerized. Accordingly, a manual search of paper records was required any time the CRCS conducted a lookback or traceback. This was slow, tedious, and prone to human error. The CBC consistently denied the CRCS state-of-the-art computer technology, which, had it been in place, would have enabled more efficient lookbacks and tracebacks, in addition to providing an integrated system to better administer donor recruitment, reporting adverse reactions, clinic planning operations, and blood product inventories.¹⁸⁹¹

¹⁸⁸⁹ Ex. 645, CRC Vol. 42, Tab 11 (Letter from Dr. Sandler to Responsible Heads, Directors/Medical Directors etc. - AmCross, dated June 20, 1986 re: Joint Statement on Lookback).

¹⁸⁹⁰ Evidence of Dr. Davey, former Assistant National Director BTS, pp. 29998-29999.

¹⁸⁹¹ Ex. 864, Vol. 196, Tab 2 (Minutes of CBC-CRC Sub-Committee Meeting on Systems, dated March 20, 1987).

1012. In its 1984 budget request, the CRCS included a five-year Electronic Data Processing (hereinafter referred to as "EDP") budget for the implementation of a blood program management information system (hereinafter referred to as "BPMIS"). This system was intended to cover all aspects of the blood programme, including Blood Product Management and Quality Assurance.¹⁸⁹² It was to track blood, not only for the purposes of lookbacks and tracebacks, but also for recalls and inventory management. The Blood Information System (hereinafter referred to as "BLIS"), in place since the 1970s to store only donor records and information, did not have the capacity to perform these tasks.

1013. The CBC obtained the services of a computer consultant to determine the economic and practical feasibility of these plans in December 1983. The consultant concluded that:

In my opinion the projected systems are already in place in organization (sic) of comparable size, and I was somewhat surprised to find the relative lack of progress in EDP at CRCS.

...

In conclusion, I was impressed by the National Systems Department and would be prepared to place my faith in the management personnel there to provide the proposed systems on time and within cost...¹⁸⁹³

1014. The CBC considered this report at its January 30, 1984 meeting. Members of the CBC were concerned that no cost/benefit studies had been undertaken. Accordingly, their governments would not commit to such a high cost expenditure. All members agreed that the CRCS presentation did not justify the proposed system and forwarded that message to the CRCS.¹⁸⁹⁴

¹⁸⁹² Ex. 736, Tab 24, p. 2 (*Letter from Mr. Fredrickson to Dr. Leclerc-Chevalier, dated December 5, 1983*).

¹⁸⁹³ *Ibid*, p. 6.

¹⁸⁹⁴ Ex. 736, Tab 27, p. 7 (*Record of Decisions of the meeting of the Canadian Blood Committee, January 30, 1984*).

1015. Notwithstanding the earlier report on the CRCS systems development, and following the VAX affair¹⁸⁹⁵, the CBC retained an outside consultant to review the CRCS proposed systems development. This review was conducted by Systemhouse Ltd. and was completed by August 1984.¹⁸⁹⁶ The CBC's consultant concluded that the CRCS should create a more detailed plan, and establish a pilot project. He also stressed that the CRCS should be provided with the necessary resources required for the Systems Development Plan. He concluded that the climate and leadership capability at the Red Cross was present to implement his recommended course of action.¹⁸⁹⁷

1016. In the 1985 budget, the CRCS received funds from the CBC to develop more detailed plans for BPMIS. These further plans were necessary to convince the funding governments of the need for automation in the blood programme.¹⁸⁹⁸

1017. The CRCS was requested to develop a comprehensive report on computer systems and submit it to the CBC as part of their 1986 systems department proposed budget.¹⁸⁹⁹

1018. On November 27, 1985 the CRCS forwarded a twenty-page status report and BPMIS Planning Project proposal to the CBC. The transmitted letter requested the Executive Director of the CBC to contact the Secretary General if she had any questions.¹⁹⁰⁰ This information was presented to the CBC at its December 16-17, 1985 meeting. The CBC decided

¹⁸⁹⁵ See discussion in Part I, Section B. *Canadian Blood Committee, Subsection d) The Vax Affair.*

¹⁸⁹⁶ Ex. 860, Vol. 192, Tab 1, p. 4 (draft *Record of Decisions of the Meeting of the Canadian Blood Committee, August 23-24, 1984*).

¹⁸⁹⁷ *Ibid*, p. 4.

¹⁸⁹⁸ Ex. 860, Vol. 192, Tab 6, p. 174 (*Record of Decisions of the meeting of the Canadian Blood Committee, January 15-16, 1985*).

¹⁸⁹⁹ Ex. 861, Vol. 193, Tab 1, p. 35 (April 26, 1985, *Letter from Dr. D. Leclerc-Chevalier to Mr. George Weber*).

¹⁹⁰⁰ Ex. 862, Vol. 194, Tab 2, p. 31 (November 27, 1985, *letter from Mr. G. Weber to Dr. D. Leclerc-Chevalier*).

that "the lack of information obtained from the CRCS did not permit it to develop an orientation on the issue."¹⁹⁰¹

1019. The question of the automation of the blood system was again addressed at the February 4-5, 1986 meeting of the CBC. As part of their submission for automation, the CRCS requested \$350,000 to implement a bar-coding system. Dr. Perrault, who fortuitously was at this meeting, explained to the CBC that the principle of the system was that the donor was identified by a bar-code which would follow through laboratory testing and distribution of the four potential components: plasma, cryoprecipitate, platelets and pocket cells, at the hospital level. The reason for this request was that the current manual system was labour-intensive and, with each transcription, there was the additional possibility of errors. Dr. Perrault also noted that the *Food and Drugs Act* required that donors be traced if it was discovered, after products were distributed, that a donor had a transmissible disease. As Dr. Perrault did not expect to discuss this item, he did not have the file with him and could not answer questions on the projected total cost.¹⁹⁰²

1020. Mme. Hebert, the Quebec representative, questioned the relevance of a bar-coding system, stating that this was not approved. She requested a cost-benefit analysis, gains and productivity analysis, and projections for the total implementing cost, before approving the 1986 budget related to bar-coding.¹⁹⁰³

1021. With respect to the general MIS hardware strategy, the members of the CBC were concerned with the strategy the CRCS was taking. It was suggested by the British Columbia representative that another cost-benefit study be undertaken where the project would be forced to pay for itself over five years. The Committee members agreed that close consultation with

¹⁹⁰¹ Ex. 862, Vol. 194, Tab 2, p. 17 (*Record of Decisions of the Canadian Blood Committee, December 16-17, 1985*).

¹⁹⁰² Ex. 862, Vol. 194, Tab 4, p. 109 (*Draft Record of Decisions of the Meeting of the Canadian Blood Committee, February 4-5, 1986*).

¹⁹⁰³ *Ibid.*

the CRCS would have to be undertaken before the CRCS proceeded to implement its MIS strategy¹⁹⁰⁴.

1022. At the June 23 to 24, 1986 meeting of the CBC, the issue of MIS was again revisited by the members. The Chairman indicated that the systems review (proposed at the earlier meeting) had not yet taken place. It was agreed that the CBC should send a strong message to the CRCS indicating that it was not prepared to spend any additional money on systems development until it received a plan that met its requirements. The CBC was not in favour of the CRCS's centralized plan. Some members suggested that the CRCS should be informed that it should deal with the CBC on the basis of "province first and national office second". One member questioned whether the CRCS needed online centralized access to donor and other information at this point, or ever. The CBC's view on this point was that the CRCS should identify its needs with respect to MIS and then the CBC Executive Committee would decide whether these were acceptable. Again the CBC determined that an outside firm should review the CRCS MIS proposed systems.¹⁹⁰⁵

1023. At the November 2 to 3, 1986 CBC meeting, the Chairman informed the Committee that the CRCS had been advised that no systems development would be supported by the CBC without its prior approval, as the CBC had decided to form a subcommittee to study the issue.¹⁹⁰⁶

1024. On March 20, 1987, the CRCS presented a preliminary umbrella plan of software and hardware required to meet the needs of the blood programme to this newly formed CBC Subcommittee on systems. The CRCS was assisted in this endeavour by the consulting firm Stevenson, Kellogg, Ernst & Whinney. The subcommittee was informed that the cost of this

¹⁹⁰⁴ *Ibid at p. 113.*

¹⁹⁰⁵ *Ex. 862, Vol. 194, pp. 188-190 (Draft Record of Decisions of the Meeting of the Canadian Blood Committee, June 23-24, 1986).*

¹⁹⁰⁶ *Ex. 863, Vol. 195, Tab 2, pp. 20-21 (Record of Decisions of meeting of the Canadian Blood Committee, November 2-3, 1986).*

system would be approximately \$12 million. The CBC denied this request. In so doing, it informed the CRCS that it did not wish the blood programme to become a major leader in systems development and implementation, while the hospitals received significantly less support in this area. Furthermore, the CBC refused to support the magnitude of the software and hardware costs involved in this system.¹⁹⁰⁷

1025. In August, 1987, a further presentation by the CRCS to the CBC met with a similar lack of success.¹⁹⁰⁸ In September, 1987, the CBC made it clear that the proposed plan formulated by the Systems Subcommittee for a fully integrated computer system was beyond the funding capacity of the CBC. A comprehensive new system would not be approved. Instead, the CRCS was asked to develop:

...a more reasonable proposal by reducing the elements to be automated and/or reducing the pace of automation implementation.

It appears to the CBC that importation of an external system tends to encourage plans for simultaneous development of the full range of capacities inherent in such an external system. While this may be seen as organizationally attractive, it is inconsistent with the orientation of governments which favours incremental financial commitment based upon a sequential pursuit of priorities.

The provinces and territories are not ready to pledge a broad multi-year multi-million dollar level of support embracing coast-to-coast implementation of comprehensive automated systems.¹⁹⁰⁹

1026. The CRCS was directed to submit a plan to the CBC which would provide for incremental improvements to the computer system CRCS was already utilizing. The CRCS communicated to the CBC that a fully integrated system was essential for safety. The history of difficulties with respect to withdrawals, recalls, and product shortages could only be

¹⁹⁰⁷ Ex. 864, Vol. 196, Tab 2, p. 13 (*Meeting of the CBC/CRCS Subcommittee on Systems, March 20, 1987*).

¹⁹⁰⁸ *Ibid*, Tab 7 (*Meeting of the CBC/CRCS Subcommittee on Systems, August 10, 1987*).

¹⁹⁰⁹ Ex. 737, Tab 5 (*Letter from Dr. Leclerc-Chevalier to Dr. Perrault, dated September 22, 1987*).

addressed by computerization, which would allow for distribution data, accuracy in tracing blood components, efficiency, timeliness, and monitoring of product.¹⁹¹⁰

1027. At the CBC/CRCS Executive Committee meeting of April 14, 1988, Dr. Perrault recounted a problem which had occurred at two AmCross centres, in an effort to convince the CBC of the possible jeopardy to the safety of the blood supply without such a system. Inspections at these centres revealed errors which resulted in the release of blood products which were not suitable for distribution. Dr. Perrault stressed that such an event was foreseeable at the CRCS, given its lack of computerization to manage data and inventories and the possibility of human error with respect to the current manual system.¹⁹¹¹ The level of scepticism by the CBC about the safety benefits of a completely automated system is evidenced in the CBC minutes of that meeting which read:

The Canadian Red Cross is pretending that inadequate computer facilities were the cause of the above events...¹⁹¹²

Mme Hebert commented that computer services does not constitute assurance against errors and that good organization is more likely to prevent errors.¹⁹¹³

1028. The CRCS continued to press for an automated information system.¹⁹¹⁴ On March 16, 1989, the CBC approved funds in the amount of \$1.5 million, over three years, for the development of a new comprehensive information system for blood centres to be piloted and

¹⁹¹⁰ Ex. 737, Tab 8 (*Memo from Dr. Walker to Dr. Perrault, Deputy Secretary General, dated December 4, 1987 re: Replacement of Factor VIII and Factor IX*).

¹⁹¹¹ Ex. 866, Vol. 198, Tab 3, p. 118 (*Minutes of the CBC/CRCS Executive Committee Meeting, dated April 14, 1988*).

Ex. 737, Tab 21 (*Position paper by Tom Walker, dated March 6, 1989 re: the Need to Automate Information Systems*).

¹⁹¹² Ex. 866, Vol. 198, Tab 3, p. 118 (*Record of Decisions of the Minutes of CBC/CRCS Executive Committee Meeting, dated April 14, 1988, paragraph 19*).

¹⁹¹³ *Ibid*, p. 118.

¹⁹¹⁴ Ex. 737, Tab 22, p. 5441101 [*March 16, 1989 Minutes of Canadian Blood Committee*].

reviewed before their funding for implementation.¹⁹¹⁵ This commitment eventually led to a plan for the implementation of Computerized Information System for Centre Operations (hereinafter referred to as "CISCO"), which is currently under way. CISCO is not expected to be fully operational until the year 2000.¹⁹¹⁶ Today, most centres are still using BLIS along with an inventory tracking system for fractionated products.

6) Broader Strategies Required

1029. CISCO will greatly increase the speed at which lookbacks and tracebacks can be conducted at CRCS centres. However, the weak link in the system had been that hospital records are incomplete and often filed according to patient name, rather than blood unit number. This had made complete lookbacks in some cases virtually impossible.¹⁹¹⁷ The CRCS defined its role and that of hospital blood banks, which was to keep records detailing the receipt and disposition of blood and blood products, in the 1983 *Clinical Guide to Transfusion*:

3. Hospital Blood Bank Responsibilities

- to discuss and offer guidance in the appropriate use of blood products;
- to maintain an adequate inventory of blood and blood products under appropriate storage conditions
- to perform compatibility testing of the donor's blood with the recipient's blood to provide maximum protection against a potentially incompatible transfusion

¹⁹¹⁵ Ex. 1077, Vol. 268, Tab 3, p. 52 (*Proposal for Funding of a Computerized Information System for Centre Operations [C.I.S.C.O.]*).

¹⁹¹⁶ Evidence of Mr. George Gargarella, COI Group Incorporated re CISCO, pp. 44325-44326.

¹⁹¹⁷ Evidence of Dr. Schroeder, Winnipeg Centre Medical Director, pp. 9913-9916;

Evidence of Dr. Herst, Toronto Centre Medical Director, pp. 21433-21434; and

Evidence of Dr. Decary, Montreal Centre Medical Director, p. 16155-59.

- to ensure that personnel in the blood bank shall have had sufficient training and experience to qualify as technically competent in the procedures performed
- to keep records that detail the receipt and disposition of all blood and blood products
- to keep records on patient testing
- to ensure that a review mechanism for blood transfusion practice is operative in the hospital
- to investigate significant transfusion reactions and submit appropriate reports to the regional blood transfusion centre as requested¹⁹¹⁸

1030. When a donor tested positive, the CRCS was able to link the name of the donor and the unit number of his/her donation with the hospital to which that unit was sent. However, hospitals were often constrained from searching for the name of the recipient by their manual record keeping, which does not allow them to search by unit number:

...the difficulty with hospital records, sir, was not their retention. Hospitals have a duty to retain records in fact, and do so over long periods. It was what they contained specifically with reference to blood transfusion.

Now, this had been noted, for example, by the Ontario Coroner in an inquest conducted about 1984 into reactions to blood platelets. And it was then noted that very often there were no records of transfusion of blood or products, or that those records did not make it -- it was difficult from those records to establish, for example, whether cross-matched blood for a given patient had actually been transfused.

Parts of the record which contained details of transfusion, such as fluid balance sheets, were routinely culled from records before they were bound for long-term retention. So to make the linkage between a blood product, blood or a product sent to a hospital, and the patient to whom it had actually been given, could be extremely difficult or impossible.

Now, beyond that point came the difficulty of then tracing that individual patient and making contact with them at a time when they had long out of touch with the hospital. That difficulty certainly increased with time.

But given the cases of AIDS and donors with HIV were detected some time after their blood was transfused, that was part of the problem from the beginning.

¹⁹¹⁸ Ex. 539, Tab 1, p. 30 (*Clinical Guide to Transfusion, Products and Practices, Second Edition, 1987*).

So the first difficulty was tracking back to the -- and finding the actual details of blood or product used, and then there were problems with actually contacting the recipient or recipients.¹⁹¹⁹

1031. The CRCS was further hindered in its investigations by the inconsistent reporting of cases of transfusion-associated AIDS by hospitals or physicians.¹⁹²⁰ In recognizing this problem, some centre Medical Directors initiated a link with physicians having anti-HIV patients who admitted to being blood donors, so that hospitals could be notified of any units sent to them from those donors. For example, in 1991 Dr. Remis compared AIDS lists with donor lists with Dr. Delage at the Montreal centre.¹⁹²¹ Dr. Turc, in Edmonton, attempted to make arrangements with the Alberta Medical Association to receive the names of anti-HIV positive donors who continued to donate despite counselling that they should not do so.¹⁹²² Dr.

¹⁹¹⁹ *Evidence of Dr. Davey, former Assistant National Director BTS, pp. 29988-29989.*

¹⁹²⁰ *Evidence of Dr. Susan King, Assistant Director, HIV/AIDS Comprehensive Care Program, Hospital for Sick Children, pp. 2518-2524; and*

Evidence of Dr. Poon, Assistant Professor, Department of Pathology, University of Toronto, p. 3887.

¹⁹²¹ *Evidence of Dr. Remis, Montreal Epidemiologist, pp. 41172-41173 and 41177-41178.*

¹⁹²² *Ex. 165, Vol. 62, Tab 59 (Letter from Dr. Turc to Dr. Perry, President of the Alberta Medical Association, dated May 27, 1986);*

Ibid, (Response from Dr. Perry to Dr. Turc, dated July 18, 1986);

Ibid, (Letter from Dr. Turc to Dr. Olhauser, College of Physicians and Surgeons, dated September 8, 1986);

Ibid, (Response by Dr. Olhauser to Dr. Turc, dated October 1, 1986);

Ibid, (Letter by Dr. Harper, Assistant Executive Director of the Alberta Medical Association, to Dr. Turner, dated January 8, 1987);

Ibid, (Response by Dr. Turner to Dr. Harper, dated January 30, 1987);

Ibid, (Letter from Dr. Harper to Dr. Turner, dated April 21, 1987); and

Evidence of Dr. Larke, Deputy Medical Director, Edmonton Centre, pp. 6579-6582.

This suggestion was seriously considered and was eventually rejected for confidentiality reasons. The Alberta Medical Association took the position that only legislated mandatory reporting of anti-HIV positive donors would not compromise the physician/patient relationship.

Buskard in Vancouver made a similar suggestion when he approached physicians and requested that a list of all patients who died of AIDS be matched against the donor list. Physicians, however, would not provide this information because of physician/patient confidentiality.¹⁹²³ Dr. Herst ran into a similar roadblock.¹⁹²⁴

1032. Studies have shown that targeted lookback is only marginally effective and therefore ought to be one part of a broader strategy.¹⁹²⁵ A California study has demonstrated that only 3-5% of recipients are identified this way,¹⁹²⁶ in part, because people are mobile and it is impossible to locate them after they have moved.¹⁹²⁷

1033. Other approaches to notifying individuals include public announcements to all possible blood transfusion recipients, direct contact of a recipient by mail or telephone, indirect contact by the recipient's physician, or comparing donor lists with lists of AIDS cases. It is generally agreed that multiple strategies are the key to success.¹⁹²⁸ Consequently, the CRCS targeted lookback program alone cannot be expected to reach all possibly infected transfusion recipients. The CRCS requires the assistance of the other players in the public health system. Throughout the 1980s, without this assistance, the CRCS made its best efforts to overcome the weak links in the system.

¹⁹²³ *Evidence of Dr. Buskard, former Vancouver Centre Medical Director, pp. 5560-5561; and Ex. 111, Vol. 47, Tab 22 (Memo from A. Adatia to Dr. Buskard, dated June 24, 1985).*

¹⁹²⁴ *Evidence of Dr. Herst, Toronto Centre Medical Director, pp. 20492-20496.*

¹⁹²⁵ *Evidence of Dr. Susan King, Assistant Director, HIV/AIDS Comprehensive Care Program, Hospital for Sick Children, pp. 2511-2514.*

¹⁹²⁶ *Ex. 52 (Article in Transfusion, dated 1990, entitled "Identification of HIV Infected Transfusion Recipients: Utility of Cross-referencing, Previous Donor Records with AIDS Case reports" by Samson et al).*

¹⁹²⁷ *Evidence of Dr. Larke, Deputy Medical Director, Edmonton Centre, pp. 6726-6728.*

¹⁹²⁸ *Evidence of Dr. Susan King, Assistant Director, HIV/AIDS Comprehensive Care Program, Hospital for Sick Children, pp. 2359-2361; and*

Evidence of Dr. Remis, Montreal Epidemiologist, pp. 41179-41181.

1034. The CRCS issued a press release dated March 17, 1987 advising that any persons who had received a blood transfusion between the years 1978 and the introduction of testing:

... for their own welfare and peace of mind and that of their loved ones, should discuss their concerns with their physician, who may recommend a test...¹⁹²⁹

Media releases have been effective in ensuring that recipients who have cause to worry get the message and consider testing, as is indicated by the number of anti-HIV tests conducted at provincial health facilities following such press releases.¹⁹³⁰ This press release was issued long before any public health authorities delivered a similar message. It is one example of the initiatives taken by the CRCS in a vacuum of public health action in response to AIDS.

¹⁹²⁹ Ex. 648, CRC Vol. 45, Tab 34 (CRCS Press Release, dated March 17, 1987).

¹⁹³⁰ Evidence of Dr. Rekart, Director of STD Control for British Columbia, Ministry of Health, pp. 4881-4882;

Ex. 98, Vol. 36, Tab 22 (September 20, 1993 Province of British Columbia News Release);

Ibid, Tab 24 (March 2, 1994 Memorandum from D. Cook, Province of British Columbia to Dr. Rekart re: HIV Test Data Tests Performed on Blood Product Recipients);

Ex. 466, Vol. 23, Pt. 4, pp. 00223-00224 (July 21, 1993 Ministry of Health, Province of Ontario News Release re: People Who Received Blood Urged to Test for HIV);

Ex. 131, Vol. 56, Tab 35 and Ex. 186, Vol. 68, p. 00321 (November 22, 1993 Province of Alberta Information Bulletin re: Recipients of Blood Transfusions (1978-1985) Advised to Have HIV Test);

Ex. 293, Vol. 88, p. 256 and Ex. 326, Vol. 89, Tab 4 (November 26, 1993 Nova Scotia Children's Hospital Press Release re: IWK supports HIV Testing);

Ex. 240, Vol. 73, Pt. 2, p. 192 (July 28, 1993 Manitoba Health Medial Bulletin re: Blood Transfusion and HIV);

Ex. 257, Vol. 83, p. 00204 (July 26, 1993 New Brunswick Press Release re: People Who Received Blood Between 1978-1985 Advised to be Tested for HIV);

Evidence of Dr. Schabas, Province of Ontario, pp. 18212-18218.

IV. THE CRCS RESPONSE TO THE THREAT OF NANB HEPATITIS

1035. Canada, unlike the U.S. in 1987, did not institute non-A, non-B ("NANB") surrogate marker testing of blood donors to reduce the risk for post-transfusion hepatitis (hereinafter referred to as "PTH"). There was a significant body of considered opinion that there was no adequate proof that surrogate testing would decrease the incidence of PTH, and secondly that the implementation HIV testing was itself a form of surrogate testing that would significantly reduce the incidence of NANB hepatitis. Rather than implement costly and unproven tests that might jeopardize the already shrinking donor base, after due consideration, the CRCS chose instead to sponsor and participate in a scientific study, specifically designed to measure the effectiveness of surrogate testing as a means of reducing the incidence of PTH in Canada. The results of this recently published study¹⁹³¹ indicated that surrogate testing would have been of limited but not insignificant value in reducing PTH incidence prior to the implementation of HCV testing. This study demonstrated that had NANB surrogate testing been implemented between 1988 and 1990, the incidence of PTH cases may have been further reduced beyond the already substantial reduction that resulted from the implementation of HIV testing. This analysis, however, was not available to the CRCS and other decision makers at the time the study was commissioned. It is the position of the CRCS that pursuing the study was both reasonable and justified given the circumstances and the information available at that time and was a reasonable exercise of judgement.

1) Historical Backdrop and Epidemiology

1036. Prior to the implementation of specific testing for hepatitis, it had been suspected that donors with liver damage might be responsible for the transmission of hepatitis in blood transfusion recipients. During the 1950's, alanine aminotransferase ("ALT"), a test designed

¹⁹³¹ Ex. 576, Vol. 137, Tab 15 (Blajchman, M. et al., "Post-transfusion hepatitis: Impact on non-A, non-B hepatitis surrogate tests." *The Lancet* January 7, 1995; 345:21-5).

to diagnose abnormal liver function, was proposed for donor screening. The conflicting observations regarding the specificity of this test, led some scientists and blood bankers to the conclusion that the effectiveness of the test had not been sufficiently established to warrant implementation.

1037. Interest in ALT testing disappeared when a specific test for serum hepatitis was described in the 1960's and implemented in the 1970's. However, this routine testing for the Hepatitis B surface Antigen ("HBsAg") in all donor blood failed to totally eliminate PTH. It was estimated that 90% of PTH was attributable to NANB hepatitis, which led to a renewed interest in the proposed use of surrogate markers for testing donor blood.¹⁹³²

1038. There was considerable uncertainty regarding the seriousness of NANB PTH as little was known about the long term effects of NANB infection until quite recently. It was a common belief among hepatitis experts that NANB hepatitis was a relatively mild disease, often with little or no residual effects. Although undesirable, it was viewed as a tolerable transfusion related risk. Medical experts did not appreciate the chronicity of NANB until the mid to late 1980's when accumulating evidence began to suggest that the clinical implications of NANB were greater than previously anticipated.¹⁹³³

¹⁹³² Ex. 579, Vol. 133, Tab 6, p. 27 (June 17, 1987 Canadian Liver Foundation/CRCS proposal: *A Controlled Clinical Trial to Determine the Efficacy and Feasibility of Screening Blood Donors for Elevated Alanine Aminotransferase (ALT) and Antibody to Hepatitis B Core Antigen (Anti HBc) as Surrogate Markers for Non-A, Non-B Hepatitis Agents in Donor Blood*).

¹⁹³³ Evidence of Dr. Zuck, former Director of Division of Blood and Blood Products, FDA, pp. 22475-22476;

Evidence of Dr. Blajchman, Hamilton Centre Medical Director, p. 22953;

Evidence of Dr. Davey, former Assistant National Director BTS, pp. 29032-29033; and

Ex. 577, Vol. 135, Tab 42, pp. 203-204 (Alter, H., "Post-transfusion Hepatitis: Clinical features, risk and donor testing." *American Red Cross Annual Scientific Symposium* May 9-11, 1984, Washington, D.C.).

1039. Given this history, and given the time and resources directed to AIDS and HIV during the early 1980's, NANB PTH was a lesser priority for transfusion experts worldwide.¹⁹³⁴ Dr. Feinman put hepatitis in its proper historical perspective:

You see it is different when somebody has cholera. In a cholera epidemic you have to decide quick. [Cholera] kills rapidly. So you can exclude a part of the city water, but in [NANB PTH] which looks not very serious, unfortunately, that is not a comparison to plague, cholera or to HIV. [NANB PTH] was a relatively benign disease in the eyes of most medical professionals.¹⁹³⁵

2) The U.S. Studies (The TTV and NIH Study Groups)

1040. Prior to Drs. Blajchman and Feinman completing their study on NANB surrogate testing,¹⁹³⁶ a few U.S. studies attempted to evaluate the efficacy of surrogate testing as a means to reduce NANB PTH. In the 1984 Canadian Liver Foundation proposal for a Canadian efficacy study, the investigators emphasized that no true efficacy study had yet been done. At best, the U.S. studies could merely *predict*, not prove, the efficacy of surrogate testing:

All of the studies described above have attempted to predict the efficacy of the use of ALT and/or anti-HBc as surrogate tests for post-transfusion Non-A, Non-B hepatitis. No true efficacy studies have been done. In other words, there have been no controlled clinical trials that have followed a group of patients who have received blood from a source that has been tested and from which the units having positive test results have been removed, and compared them to a group of patients who have received blood from a source which has not been tested.¹⁹³⁷

¹⁹³⁴ Evidence of Dr. Blajchman, Hamilton Centre Medical Director, and Evidence of Dr. Feinman, Co-Director, Hepatitis Research Laboratory, The Toronto Hospital, pp. 22951-23001.

¹⁹³⁵ Evidence of Dr. Feinman, Co-Director, Hepatitis Research Laboratory, The Toronto Hospital, pp. 22959-22960.

¹⁹³⁶ Ex. 576, Vol. 137, Tab 15 (Blajchman, M. et al., "Post-transfusion hepatitis: Impact on non-A, non-B hepatitis surrogate tests." *The Lancet* January 7, 1995; 345:21-5).

¹⁹³⁷ Ex. 579, Vol. 133, Tab 6, p. 28 (June 17, 1987 Canadian Liver Foundation/CRCS proposal: A Controlled Clinical Trial to Determine the Efficacy and Feasibility of Screening Blood Donors for Elevated Alanine Aminotransferase (ALT) and Antibody to Hepatitis B Core Antigen (Anti HBc) as Surrogate Markers for Non-A, Non-B Hepatitis Agents in Donor Blood);

1041. The first of these U.S. studies, The Transfusion - Transmitted Viruses Study⁹³⁸ ("the TTV study") was published in 1981. In it Dr. Aach et al. predicted that ALT screening could reduce NANB PTH incidence by approximately 37%. However, Dr. Aach's study acknowledged ALT's lack of sensitivity and poor specificity.

1042. Later in 1981, a study by Dr. Alter et al.⁹³⁹ of the National Institutes of Health ("the NIH study") predicted that ALT testing of donors could prevent up to 29% of PTH with a 1.6% loss of donor units. The authors acknowledged that ALT testing was "a tenuous balance between risk and benefit" and that in light of the non-specificity of the test and the substantial cost of implementing it, a randomized clinical trial was required.

1043. A continuation of the TTV study was published in 1984⁹⁴⁰ and predicted that combined ALT and anti-HBc surrogate testing could reduce NANB PTH by approximately 61% with a donor loss of approximately 8%. The authors concluded that ALT was more efficacious and less costly than anti-HBc, and recommended that the ALT test alone should be used.

1044. In 1986, the NIH study group published a further study that essentially corroborated the earlier TTV and NIH studies. This second NIH study predicted that excluding anti-HBc positive donors might prevent 43% of NANB PTH cases with a donor loss of 4%. However, the authors did point out various key problems associated with using ALT and anti-HBc as surrogate tests:

See also Evidence of Dr. Blajchman, Hamilton Centre Medical Director, pp. 22962-22963.

⁹³⁸ Ex. 577, Vol. 135, Tab 24 (Aach, R. et al., "Serum alanine aminotransferase of donors in relation to the risk of non-A, non-B hepatitis in recipients: The Transfusion - Transmitted Viruses Study." NEJM April 23, 1981; 304(17):989-94).

⁹³⁹ Ex. 577, Vol. 135, Tab 27, p. 149 (Alter, H. et al., "Donor transaminase and recipient hepatitis. Impact on blood transfusion services." JAMA August 7, 1981; 246(6):630-4).

⁹⁴⁰ Ex. 577, Vol. 135, Tab 48, pp. 273-274 (Stevens, C. et al., "Hepatitis B virus antibody in blood donors and the occurrence of non-A, non-B hepatitis in transfusion recipients: An analysis of the Transfusion - Transmitted Viruses Study." Annals of Internal Medicine December 1984; 101(6):733-8).

Both have a relatively low level of predicted efficacy in preventing non-A, non-B hepatitis, and 60% to 70% of non-A, non-B transfusion-associated hepatitis will probably continue to occur despite implementation of either of these tests. Equally disturbing, both tests have a high rate of false positivity: 70% to 88% of recipients of blood with anti-HBc or an elevated ALT level do not develop non-A, non-B hepatitis, and approximately 60% of donors with elevated ALT levels have nonviral factors as the most likely cause of their transaminase elevation. An additional major concern is the resultant loss of blood donors, estimated to be 1% to 3% for ALT elevations and 4% to 8% for anti-HBc.¹⁹⁴¹

Despite these many problems, the authors nevertheless recommended that surrogate testing be implemented. Concerned with the high percentage of PTH patients that developed chronic hepatitis and cirrhosis, they concluded that the interest of disease prevention outweighed the disadvantages associated with adoption of NANB surrogate testing.

1045. Dr. Mosely, who was one of the investigators in the TTV studies, testified that, in his opinion, routine ALT screening should have been implemented in the U.S. and in Canada by the end of 1981 after the first NIH study confirmed the initial TTV results.¹⁹⁴² His opinion, however, was not widely accepted during this timeframe. In the U.S., various experts viewed the TTV data as inconclusive and advocated that a proper efficacy study be carried out.

1046. In the report of the *ad hoc* committee on ALT testing¹⁹⁴³, Bove et al. clearly rejected the proposition of routine ALT testing. Citing various factors including lack of specificity and the negative impact on the donor base with the potential for severe blood shortages, the authors were unconvinced that the available evidence justified universal ALT testing of donor blood. The authors also stressed the need for a properly designed study that did more than provide correlation data that merely suggested a reduction in NANB PTH as a result of ALT screening:

¹⁹⁴¹ Ex. 583, Vol. 136, Tab 3, p. 10 (Koziol, D. et al., "Antibody to hepatitis B core antigen as a paradoxical marker for non-A, non-B hepatitis agents in donated blood." *Annals of Internal Medicine* April 1986; 104(4):488-95).

¹⁹⁴² Evidence of Dr. Mosely, *Pediatrician, Hemophiliac Treater*, pp. 25707-25709.

¹⁹⁴³ Ex. 577, Vol. 135, Tab 29 (Bove, J.R. et al., "Report of the *ad hoc* committee on ALT testing (June 15, 1981)." *Transfusion* 1982; 22(1):4-5).

No study has shown that the actual elimination of donors with elevated levels of ALT will reduce the incidence of elevated levels of ALT post-transfusion, much less hepatitis. Current studies correlate donor levels of ALT with post-transfusion levels in the recipient. It is essential to show that elimination of donors with high levels of ALT will, as postulated, reduce the number of recipients who also have high levels. Such studies must be done before drastic changes in donor qualifications can be justified ...

... we believe that the best interests of the many patients who depend on a reliable supply of blood are best served by continued investigation rather than a change in donor eligibility standards.¹⁹⁴⁴

1047. It is worth noting that Drs. Alter and Holland, both of whom formed part of the NIH study group, were sceptical of the initial TTV data. In a 1983 letter to the New England Journal of Medicine, these prominent U.S. experts emphasized the need for a properly designed scientific study:

There are no prospective, randomized, controlled trials that prove that the predicted efficacy of ALT screening can be realized ... Neither the ad hoc committee report on ALT testing nor the major blood-banking organizations have recommended the routine use of ALT screening for the prevention of non-A, non-B transfusion-associated hepatitis at this time. More information is needed and is being sought.¹⁹⁴⁵

1048. In another article published during this time, Dr. Holland also pointed out some of the technical problems associated with ALT screening. Commenting on previous studies including the initial TTV and NIH studies, Dr. Holland noted the following:

... the majority of transfusion-associated hepatitis occurred in recipients of blood which did not have an elevated ALT. In fact, rejection of elevated ALT blood would not have eliminated 70% or more of the hepatitis in these studies. In addition, in each study, most patients who received blood with an elevated ALT did not develop hepatitis ... So, the second problem with the ALT test is that it is too nonspecific to be used routinely as a screening test to identify hepatitis

¹⁹⁴⁴ *Ibid* at pp. 151-152.

¹⁹⁴⁵ Ex. 728(A) (Alter, H.J. and Holland, P.V., "Donor Serum Alanine Aminotransferase Activity and the Risk of Transfusion - Associated Hepatitis". *NEJM* March 24, 1983; 308(12):723 Reprinted in *Plasma Quarterly*, Fall 1983; 5(3):92);

Ex. 577, Vol. 135, Tab 32, p. 157 (June 2, 1982 Inter-Agency Technical Committee Working Group on Blood Resources and Blood Substitutes Meeting as reported in the June 4, 1982 AABB Government Affairs Update).

carriers among blood donors; it has too many "false-negatives" and too many "false-positives".¹⁹⁴⁶

1049. In 1984, Drs. Alter and Holland renewed their call for a properly designed scientific study:

The third option is that existing data are inconclusive, but are sufficiently compelling that a definitive answer must be sought. Implicit is the assumption that efficacy based on predictions from a nonrandomized study is not the same as efficacy established by a randomized, controlled trial ... Although it may be construed as unethical to withhold a given interventive measure, history has shown that it may be equally unethical to withhold the proper study; a randomized, controlled study should be instituted as rapidly as possible.

It is our opinion that the third option is the most tenable alternative.¹⁹⁴⁷

1050. This message was reinforced over a year later in a statement by Dr. Zuck at the American Blood Commission Board of Directors meeting in March 1986 when he stated, "The bottom line is, we need a long term, prospective study".¹⁹⁴⁸

3) Scientific Literature Refuting U.S. Data

1051. The data from the U.S. studies were not universally accepted. The "predicted" value of surrogate testing for NANB was viewed by many international transfusion experts as controversial. Several studies refuted the TTV and NIH data bringing into question the validity of the U.S. studies. These various studies are briefly discussed below.

¹⁹⁴⁶ Ex. 577, Vol. 135, Tab 37, p. 179 (*International Forum*, "Based on your analysis of the benefits and costs of routine donor screening for ALT-GPT to reduce the incidence of post-transfusion non-A, non-B hepatitis in your blood services region, what action would you recommend on this matter?" *Vox Sanguinis* 1983:48-64).

¹⁹⁴⁷ Ex. 577, Vol. 135, Tab 49, p. 278 (Alter H.J., Holland P.V., "Indirect tests to detect the non-A, non-B hepatitis carrier state." [editorial] *Annals of Internal Medicine* December 1984; 101(6):859-61).

¹⁹⁴⁸ Ex. 722, p. 2 (March 14, 1986 CCBC Newsletter).

1052. In a 1983 study of Montreal transfusion recipients, Steinbrecher et al. sought to evaluate ALT as a potential surrogate test for NANB PTH. The authors concluded that the risk of NANB PTH was the same in recipients of blood with elevated ALT levels as in those who received blood with normal ALT levels. Thus, the study failed to establish a correlation between elevated ALT levels in donors, and PTH in recipients.¹⁹⁴⁹ Much like Drs. Alter and Holland and other international experts, the authors of this Canadian study were cautious about the prospect of routine ALT donor screening:

Until a sensitive and specific test for non-A, non-B hepatitis is developed, any non-specific screening test, such as ALT measurement, must be carefully evaluated in the population where its introduction is being considered.¹⁹⁵⁰

1053. In a 1986 study of transfusion recipients in France, Aymard et al attempted to assess anti-HBc in donor blood as a surrogate marker for NANB PTH. The authors found that units of blood from anti-HBc positive donors were not associated with a greater risk of NANB PTH. No case of NANB hepatitis developed among the patients who received blood from anti-HBc positive donors and the authors noted that 4.5% of donors would therefore have been discarded without any reduction in the incidence of NANB PTH in recipients. The authors concluded that anti-HBc testing was of no value as a screening method to reduce NANB PTH.¹⁹⁵¹

1054. In a 1986 letter to the editor of the *Annals of Internal Medicine*, the authors of a Spanish study stated that in contrast to the 1986 NIH study, their results did not support the use of anti-HBc as a surrogate marker.¹⁹⁵²

¹⁹⁴⁹ Ex. 576, Vol. 137, Tab 7 (Steinbrecher, U. et al., "Abnormal alanine aminotransferase level in blood units from donors in Montreal does not indicate high risk of transmitting hepatitis." *Clinical and Investigative Medicine* 1983; 6(4):327-30).

¹⁹⁵⁰ *Ibid* at p. 23.

¹⁹⁵¹ Ex. 576, Vol. 137, Tab 26 (Aymard, J. et al., "Post-transfusion non-A, non-B hepatitis after cardiac surgery." *Vox Sanguinis* 1986; 51:236-8).

¹⁹⁵² Ex. 584, Tab 1 (Hoyos, M. et al., "Markers for Non-A, Non-B Hepatitis." [letter to editor] *Annals of Internal Medicine* 1986; 105:467).

1055. In their 1988 study of Scottish transfusion recipients, Gillon et al.¹⁹⁵³ examined the significance of elevated ALT and anti-HBc in blood donors. The authors found that 2.4% of donors had an elevated ALT, but 82% of these donors had a non-viral explanation for their abnormal test results, the majority being due to alcohol and obesity. The authors were critical of the design of the TTV and NIH studies noting that they were flawed by major statistical bias. While they acknowledged that the U.S. data was adequate to demonstrate a statistically significant association between elevated ALT levels and recipient NANB PTH, the authors of the Scottish study claimed that the U.S. studies failed to quantify that relationship adequately. The Scottish authors concluded that in view of the medical and economical implications of the introduction of surrogate tests, and the poverty of data on the clinical significance of NANB PTH, surrogate testing was not justified. They stated:

We conclude that the introduction of these screening tests cannot at present be justified. Further studies of recipient NANB hepatitis and the natural history of the disease are necessary, and a properly conducted prospective trial of screening for surrogate markers is essential. More extensive studies of the donor population would be valuable ... Such studies would prove useful in the management of donors, should the case for screening ever be well enough established for its introduction to be considered necessary.¹⁹⁵⁴

1056. An Italian study, reported by Aneloni et al at the September 1989 International Symposium on HCV, assessed the relevance of ALT and anti-HBc as surrogate tests for the prevention of NANB PTH in relationship to the new HCV test. The abstract from this study indicated that no significant correlations were found between HCV results and anti-HBc or ALT values. The preliminary results reported in this study indicated that in a northern Italy population, anti-HBc positivity and/or elevated ALT levels could not identify donors at increased risk of transmitting NANB (HCV) PTH.¹⁹⁵⁵

¹⁹⁵³ Ex. 576, Vol. 137, Tab 45 (Gillon, J. et al., "Post-transfusion non-A, non-B hepatitis: Significance of raised ALT and anti-HBc in blood donors." *Vox Sanguinis* 1988; 54:148-53).

¹⁹⁵⁴ *Ibid* at p. 149.

¹⁹⁵⁵ Ex. 584, Tab 2 (Aneloni, V. et al., "Relationship Between Surrogate Tests for Prevention of NANB Post-Transfusion Hepatitis and Anti-HCV", *International Symposium on HCV, Rome, September 14-15, 1989*).

1057. Despite the U.S. move to implement surrogate testing in 1986 - 1987, there were subsequent studies in that country which cast doubt on that decision. A study from the Memorial Blood Centre of Minneapolis studied the prevalence of anti-HBc in the local donor population and evaluated the tests available for anti-HBc screening. Based on their data, the authors concluded that anti-HBc was a questionable surrogate test for NANB hepatitis:

Based on the correlation of anti-HBc with NANBH reported in published studies, we would have expected that previously donated blood from several of the reactive donors would have been given to patients who developed transfusion associated hepatitis. In fact, although 348 (72.2%) of the reactive donors previously had donated a total of 2877 times ... only one donor was implicated in transfusion associated NANBH.¹⁹⁵⁶

1058. In a study conducted by the American Red Cross Blood Services, Los Angeles-Orange Counties Region, Spurling et al. reviewed the problems associated with ALT testing since its implementation and concluded:

Although measurement of ALT levels has been widely used by blood banks for over 2 years, we have learned little - if anything - about its effectiveness as a surrogate test for NANB hepatitis.¹⁹⁵⁷

The authors echoed the concern of the CRCS regarding the sufficiency of data and the negative impact on the donor base:

We are aware of no published objective studies that demonstrate a clear benefit of ALT testing under the present circumstances. Alter found no reduction in NANB PTH after the introduction of ALT testing ...

Of even greater concern than cost is the fact that 3757 donors have been deferred permanently, the majority of them in their most active donor years. In these days of struggling to keep donations at last year's level and with the

¹⁹⁵⁶ Ex. 583, Vol. 136, Tab 11, p. 48 (Hanson, M. et al., "Evaluation of routine anti-HBc screening of volunteer blood donors: A questionable surrogate test for non-A, non-B hepatitis." *Transfusion* January/February 1987; 27(1):107-8).

¹⁹⁵⁷ Ex. 583, Vol. 136, Tab 27, pp. 136-137 (Spurling, C. et al., "Controversies in transfusion medicine: Alanine aminotransferase screening of blood donors: Con." *Transfusion* May 1990 30(4):368-73).

increasing frequency of serious seasonal blood shortages, we face the possibility of dire consequences that could far outweigh any benefit of ALT testing.¹⁹⁵⁸

1059. In addition to the scientific studies discussed above, there were numerous examples of transfusion specialists throughout the world who wrote about the dangers of pursuing surrogate testing without better data supporting its efficacy.¹⁹⁵⁹

1060. In a 1983 article in *Vox Sanguinis*, Dr. Robert Gerety from the Bureau of Biologics in Bethesda, Maryland put forth a view that was striking in its similarity to the position adopted by the CRCS:

No prospective study has demonstrated that eliminating donors with elevated ALT would reduce the incidence of either elevated ALT or PTH NANB in recipients.

... Studies to evaluate these alternative approaches have not yet been accomplished. There appear to be more questions than answers regarding ALT screening. Only after the answers become known can a decision be made regarding the value of ALT screening or of other non-specific measures to reduce the incidence of NANB ...¹⁹⁶⁰

1061. In the same journal, Dr. William Bayer, Director of the Community Blood Centre of Greater Kansas City set out his reasons for not pursuing ALT testing. He noted that:

... we have no real knowledge of the long-term effect of mild or intermittent transaminitis in the single transfusion episode patient ... the evidence for implementation of ALT testing on medical or public health grounds is still weak.¹⁹⁶¹

¹⁹⁵⁸ *Ibid* at p. 137.

¹⁹⁵⁹ Ex. 577, Vol. 135, Tab 37 (*International Forum*, "Based on your analysis of the benefits and costs of routine donor screening for ALT-GPT to reduce the incidence of post-transfusion non-A, non-B hepatitis in your blood services region, what action would you recommend on this matter?" *Vox Sanguinis* 1983:48-64).

¹⁹⁶⁰ *Ibid* at pp. 177-178.

¹⁹⁶¹ *Ibid* at p. 175.

Dr. Bayer also pointed out that there were cost factors which could not be ignored. In addition to the basic cost of tests, there were many hidden expenses involved in a routine ALT screening program:

Other costs for the collecting agency would include the cost for the blood and components discarded; the cost of increased recruiting to replenish supply; and the cost of time and money in explanation to 2-3% of all blood donors.

The latter may well be the most significant in cost, if not to the collection agency then to society. These donors may seek additional medical follow-up from their own physicians, which would not only increase the amount of money expended but would also create anxiety and emotional distress for many people for no real reason.¹⁹⁶²

1062. Dr. R. Mitchell, Director of the Glasgow and West of Scotland Blood Transfusion Service was also concerned about the poor performance of ALT testing and the deleterious effects it would have on blood donors and their families:

... we have no intention of suspending 3% of our volunteer blood donors on the basis of an [ALT] test when they may have only transient elevations. Furthermore, such a policy would discourage donor recruitment among the few willing to donate for the good of the community and would cause some anxiety in donors and their families when we cannot offer anything more than the argument that NANB hepatitis may exist.

... The use of nonspecific tests such as [ALT] can have deep sociological and psychological effects on established blood donors and would necessitate the recruitment of voluntarily nonremunerated replacements.¹⁹⁶³

1063. Much like the CRCS, Dr. D.B.L. McClelland, Director of the Edinburgh South-East-Scotland, Regional Blood Transfusion Service was firmly of the view that good data on incidence and efficacy were required before a rational decision on surrogate testing could be made:

... there should be a thorough prospective study to determine the frequency with which post-transfusion hepatitis occurs in the regions served by this centre ...

¹⁹⁶² *Ibid at pp. 175-176.*

¹⁹⁶³ *Ibid at pp. 181-182.*

If the results of such a study indicate that post-transfusion hepatitis due to non-A, non-B viruses (PTH) occurs sufficiently frequently to cause concern, I would recommend further study be carried out to determine whether the introduction of a donor ALT screening programme does in fact reduce the attack rate for PTH. As an alternative, it may well be possible to study simultaneously the attack rate for PTH in the recipients of ALT screened or non-screened blood.

I consider that without undertaking thorough studies along these lines, the potential and actual scale of the "benefit" side of the cost benefit calculation is unknown and therefore no rational decisions can be taken ...

I would therefore recommend that we are careful to establish the benefits *before* we become committed to the costs. We must know what improvement in the quality of our blood and blood products we are asking the community to pay for.¹⁹⁶⁴

1064. Like Canada, England did not implement NANB surrogate testing during the 1980's. Dr. John Barbara, Medical Director of the North London Blood Transfusion Centre summarized the British position in a 1987 letter to *The Lancet* editor:

Before we are forced to accept two screening tests of unproven benefit, which have high revenue implications, we need a national study to assess the incidence of raised ALT and anti-HBc in donors in different parts of the country. Also, and perhaps more importantly, a study is needed to assess the incidence of acute post-transfusion NANB hepatitis and to assess how many of those affected develop evidence of chronicity and serious clinical sequelae.¹⁹⁶⁵

1065. In a subsequent article in 1991, Dr. Barbara et al. wrote about resisting the pressures to adopt surrogate testing without sufficient data supporting their implementation:

... we felt the pressure of some clinicians demanding such tests in the UK. However, testing for non-specific surrogate markers results in unnecessary donor loss at substantial cost to the transfusion service ...¹⁹⁶⁶

¹⁹⁶⁴ *Ibid* at p. 181.

¹⁹⁶⁵ Ex. 576, Vol. 137, Tab 21 (Barbara, J. et al., "Surrogate testing for non-A, non-B hepatitis." [letter to the editor] *The Lancet* April 18, 1987:912).

¹⁹⁶⁶ Ex. 576, Vol. 137, Tab 24, p. 74 (Barbara, J. et al., "Low incidence of non-A, non-B post-transfusion hepatitis in London confirmed by hepatitis C virus serology." *The Lancet* March 30, 1991; v337:753).

1066. A 1989 Council of Europe survey indicated that the majority of European countries polled did not have a routine surrogate testing program in place. These countries included Denmark, Finland, Ireland, Netherlands, Norway and the UK. Clearly the CRCS was not alone in its decision not to implement surrogate tests for NANB hepatitis.¹⁹⁶⁷

4) Role of Dr. Feinman's Study

1067. Dr. Feinman published a study in 1988 based on data collected between 1983 - 1985 that indicated a NANB PTH incidence rate of 9.2% in Southern Ontario, a finding similar to the rates indicated in various U.S. studies during the 1970's.¹⁹⁶⁸ As was indicated in the testimony of Drs. Blajchman/Feinman and Drs. Perrault/Davey, the "true" incidence rate in Canada was thought to be considerably lower. Dr. Feinman's study was based on data collected prior to CRCS to donor screening improvements and the subsequent implementation of anti-HIV testing, and it was thought that these measures had significantly reduced the NANB PTH rate in Canada in the absence of NANB surrogate testing.¹⁹⁶⁹

1068. The CRCS and others reasonably thought that Canadians were already reaping the benefits of increased safety without the implementation of scientifically unproven surrogate tests. Although there were no scientific studies specifically designed to test this hypothesis, it was a view that was widely held by numerous transfusion experts. In his NHRDP review of the Blajchman/Feinman proposal, Dr. William Kline, American Red Cross Technical Director of the St. Paul Regional Blood Services alluded to this in his statement:

¹⁹⁶⁷ Ex. 747, (Council of Europe, Committee of Experts in Blood Transfusion and Immuno-Haematology, Liege May 23-26, 1989, "NANB hepatitis: Analysis of replies to questionnaire").

¹⁹⁶⁸ Ex. 576, Vol. 137, Tab 10 (Feinman, S. et al., "Post-transfusion hepatitis in Toronto, Canada." Gastroenterology August 1988: 95:464-9).

¹⁹⁶⁹ Evidence of Dr. Blajchman, Hamilton Centre Medical Director, and Evidence of Dr. Feinman, Co-Director, Hepatitis Research Laboratory, The Toronto Hospital, pp. 23013-23016;

Evidence of Dr. Perrault, former National Director BTS, and Evidence of Dr. Davey, former Assistant National Director BTS, pp. 29103-29105.

... [the Feinman study] was performed some time ago and the incidence of transmitters of NANB hepatitis in the donor population may not be the same (and would be likely to be lower) now.¹⁹⁷⁰

1069. In his review of the Blajchman/Feinman proposal Dr. Boucher wrote:

In addition, it is anticipated that there will be a further reduction in the incidence of post-transfusion hepatitis as an indirect consequence of donor testing for antibody to HIV (AIDS) virus and other trends (eg self-exclusion) in the blood donation practice. As I understand, the study by Dr. Feinman was conducted prior to testing for antibody to HIV virus. If this is correct, one can expect that there will be a further reduction in the incidence of post-transfusion hepatitis in the study population.¹⁹⁷¹

Dr. Boucher also noted the lack of a control group to correct for background NANB hepatitis, lending further support to the belief that the infection rate cited in Dr. Feinman's study was overestimated.¹⁹⁷²

1070. The authors of the 1986 NIH study acknowledged this factor as well:

The anticipated reduction in the incidence of transfusion-related hepatitis as an indirect consequence of donor testing for antibody to the human T-lymphotropic virus type III and other trends in blood donation practice would necessitate a substantial increase in the number of study participants to confirm the predicted efficacy of anti-HBc testing.¹⁹⁷³

1071. Dr. Alter supported this theory. In a 1989 article he wrote:

¹⁹⁷⁰ Ex. 578, Tab 34, p. 6 (*Review of the research funding proposal for the project entitled: Prevention of non-A, non-B post-transfusion Hepatitis by screening Donor Blood for anti-HBc and ALT: A prospective, randomized, double-blind controlled trial*).

¹⁹⁷¹ Ex. 578, Tab 38, pp. 2-3 (*June 30, 1988 memo from Dr. Boucher, Chief, Blood Products Division to Katherine Stewart, Project officer, Research Administration Division, Extramural Research Programs Directorate re: Prevention of non-A, non-B post-transfusion hepatitis by screening donor blood for anti-HBc and ALT: A prospective randomized, double-blind controlled trial*).

¹⁹⁷² *Ibid* at p. 2.

¹⁹⁷³ Ex. 583, Vol. 136, Tab 3, p. 10 (Holland, P. et al., "Antibody to hepatitis B core antigen as a paradoxical marker for non-A, non-B hepatitis agents in donated blood." *Annals of Internal Medicine* April 1986; 104(4):488-95).

... although there is no prospective study that has documented the impact of surrogate testing; it has been the uniform experience of the blood bank community that transfusion-associated hepatitis is increasingly rare. This cannot be solely attributed to surrogate testing, because all the measures introduced to prevent transfusion-transmitted AIDS have also had a profound effect on the apparent reduction of transfusion-associated hepatitis. It is difficult to sort out the relevant importance of these measures, but it is also difficult to escape the contention that each has played an important role.¹⁹⁷⁴

1072. This theory was borne out by subsequent data demonstrating that Canada's NANB PTH rate compared favourably with the U.S. rate during the same time period (1986-1990) without surrogate testing. Data from the Blajchman/Feinman study indicated that the incidence of NANB PTH in Canada dropped from 9.2% in 1985 to less than 1.5% by 1990. A 1990 estimate by the American Red Cross, AABB and CCBC placed the U.S. NANB PTH incidence rate in the range of 1 - 4%. Although the Blajchman/Feinman study concluded that surrogate testing would have been beneficial if implemented in Canada, it also confirmed that the vast reduction in NANB PTH came as a result of improved donor screening and anti-HIV testing. The additional cases of PTH that would have been prevented with surrogate testing would have been within that residual 1%.¹⁹⁷⁵

¹⁹⁷⁴ Ex. 579, Vol. 133, Tab 68, p.3 (Alter H.J., "Discovery of the non-A, non-B hepatitis virus; the end of the beginning or the beginning of the end". *Transfusion Medicine Reviews* III, no. 2, 1989; pp. 77-81 as excerpted in the July 10, 1989 letter from Dr. Perrault to Dr. Houser);

Ex. 571, Vol. 132, Tab 47, para no. 14 (November 1, 1985 joint NHF/CHS MSAC Minutes); and

Ex. 566, Vol. 138, Tab 10, para no. 5 (September 11-12, 1986 FDA BPAC Minutes).

¹⁹⁷⁵ Evidence of Dr. Blajchman, Hamilton Centre Medical Director, and Evidence of Dr. Feinman, p. 23273;

Ex. 584, Tab 7 (Blajchman M.A., Feinman S.V. et al., "The Incidence of Post-Transfusion Hepatitis". [letter to editor] *NEJM* April 29, 1993); and

Ex. 583, Vol. 136, Tab 25 ("Joint statement on the introduction of testing volunteer blood donors for hepatitis C virus infection." American Association of Blood Banks, American Red Cross and Council of Community Blood Centres April 30, 1990).

5) **The Importance of a Properly Designed Scientific Study**

1073. Even if the CRCS had favoured a move to ALT and/or anti-HBc testing, it was well aware that CBC funding approval for the substantial costs of these tests would have been contingent upon solid evidence demonstrating the efficacy of surrogate tests. Based on past experience with funding matters, the CRCS knew the CBC standard of proof to be extremely high. The CRCS was not so naïve as to think that the CBC would approve a costly testing program, the efficacy of which remained controversial, merely on the basis that some considered it prudent to follow the United States example. Both Drs. Davey and Perrault testified about the substantial problems associated with justifying the costs of implementing surrogate tests on the one hand, and the costs of a proposal to study their efficacy on the other. These concerns reflected the frustrating reality of operating a national transfusion service within a multiparty blood system where the real decision making power often resided outside the CRCS.¹⁹⁷⁶ Dr. Perrault made it quite plain:

We are not spending our money; let's be very clear on that. We are spending the money of these people, and I have got to convince them, not us.¹⁹⁷⁷

1074. This reality was confirmed in the evidence of the CBC Advisory panel members. On the issue of the CRCS's desire to conduct a proper efficacy study, Dr. Sullivan testified:

If Dr. Growe had been able to present definitive data to the Advisory Sub-Committee, I anticipate the Advisory Sub-Committee would have made a recommendation through me, as Chairman, to take that issue to the Canadian Blood Committee.¹⁹⁷⁸

... we agreed that the study still should [go ahead], the evidence that supported it in the first place was still valid and we ... needed to have definitive

¹⁹⁷⁶ Evidence of Dr. Davey, former Assistant National Director BTS, p. 29211.

¹⁹⁷⁷ Evidence of Dr. Perrault, former National Director BTS, p. 29251.

¹⁹⁷⁸ Evidence of Dr. Sullivan, Medical Director of Employee Health, Nova Scotia, p. 38380.

information on whether this reduced the risk of post-transfusion NANB or not.¹⁹⁷⁹

1075. In response to the Commissioner's question whether definitive scientific proof, beyond a reasonable doubt, was necessary before pursuing a public health measure, Dr. Sullivan stated:

... in the scientific community, definitive proof may vary ... Clearly, it should be statistically, on a valid prospective randomly-controlled study. There should be a statistically significant difference.

But in relation to your premise that because the United States was doing it and Europe was doing it, "Was that sufficient?", No. It was important, it was considered, but it was not sufficient.¹⁹⁸⁰

1076. Dr. Houser testified that the various countries that implemented surrogate testing made their decisions based upon "empirical" evidence based more on observation and common sense than "hard scientific evidence".¹⁹⁸¹ He stated:

The purpose of funding the study as quickly as possible was to get on with the study so we had the evidence. And the evidence would provide information that would allow the Red Cross to decide whether to recommend, or not, surrogate testing to the CBC.¹⁹⁸²

1077. As late as August, 1989 the Minutes of a CBC meeting via conference call to discuss the issue of NANB hepatitis testing summarized the situation as follows:

Jo Hauser summarized the issue for the members. There is considerable uncertainty among scientists as to the value of surrogate testing in preventing the transmission of NANB Hepatitis in transfusions.¹⁹⁸³

¹⁹⁷⁹ Evidence of Dr. Sullivan, Medical Director of Employee Health, Nova Scotia, pp. 38529-38530.

¹⁹⁸⁰ Evidence of Dr. Sullivan, Medical Director of Employee Health, Nova Scotia, p. 38533.

¹⁹⁸¹ Evidence of Dr. Houser, Executive Director, CBC, 1989-1991, pp. 38438-38606.

¹⁹⁸² Evidence of Dr. Houser, Executive Director, CBC, 1989-1991, p. 38606.

¹⁹⁸³ Ex. 867, Vol. 199, Tab 7, p. 205 (Minutes of CBC Conference Call dated August 22, 1989).

1078. Like the CBC, the BoB was not accustomed to accepting propositions based on anything less than conclusive scientific data. When speaking of the U.S. studies, Dr. Boucher stated:

... we were not convinced that in Canada that those tests would be a benefit.

... I think there is a question that there may be an association, but there certainly isn't a cause-effect that was ever established with the test.¹⁹⁸⁴

1079. On December 8, 1987 Dr. Boucher from the BoB was invited to attend the CBC meeting to address the issue of NANB surrogate testing. In discussing the possibility of a study to assess the usefulness of ALT testing in Canada, Dr. Boucher was reported to have stated in the Minutes:

It is possible, according to Dr. Boucher, that blood lacking HB core antibody may be more hazardous than blood containing it. ALT (enzyme) elevation signifies only that the donor has experienced some form of liver damage. NHROP will examine the project with its own reference.¹⁹⁸⁵ [Emphasis original]

1080. A further discussion during this meeting is reported as follows:

In response to a question from the Chairman, Dr. Boucher stated that the Bureau of Biologics would probably not order surrogate testing unless there were clear and tangible proof of increased protection. In fact, the Bureau would have concerns regarding HBc testing unless the valuable hepatitis B antibodies could be maintained in the plasma pool. This opinion will be transmitted to the NHRPD.¹⁹⁸⁶

1081. In his testimony, Dr. Furesz expressed this view:

¹⁹⁸⁴ *Evidence of Dr. Boucher, BoB Panel, pp. 43397-43406.*

¹⁹⁸⁵ *Ex. 865, Vol. 197, Tab 6, p. 15346 (Minutes of the CBC Meeting December 8, 1987).*

¹⁹⁸⁶ *Ibid.*

... my opinion was that there was no evidence, as I pointed out before, that the ALT is really going to reduce the post-transfusion hepatitis in Canada.¹⁹⁸⁷

He compared studies that produced hard data and demonstrable results with those, like the American studies, that generated speculative data. He summarized this comparison in his blunt statement, "That is science, the rest is only hearsay."¹⁹⁸⁸

1082. Support for the CRCS decision to pursue an efficacy study came from other sources as well. The Canadian Liver Foundation participated in the early stages drafting a proposal¹⁹⁸⁹ for the efficacy study that was eventually completed by Drs. Blajchman and Feinman. Once completed, the study proposal received accolades from the NHRDP and its independent referees,¹⁹⁹⁰ including Dr. Zuck who wrote, "This proposal deserves a merit score of 5 [the highest] it is a vitally needed study."¹⁹⁹¹

¹⁹⁸⁷ Evidence of Dr. Furesz, Bob Panel, pp. 43419-43420.

¹⁹⁸⁸ Ibid at p. 43421.

¹⁹⁸⁹ Ex. 579, Vol. 133, Tab 6 (June 17, 1987 Canadian Liver Foundation/CRCS proposal: A Controlled Clinical Trial to Determine the Efficacy and Feasibility of Screening Blood Donors for Elevated Alanine Aminotransferase (ALT) and Antibody to Hepatitis B Core Antigen (Anti HBc) as Surrogate Markers for Non-A, Non-B Hepatitis Agents in Donor Blood).

¹⁹⁹⁰ Ex. 578, Tab 35 (CRCS Proposal: Prevention of Non-A, Non-B Post-Transfusion Hepatitis by Screening Donor Blood for Anti-Hbc and ALT: A Prospective, Radomized, Double-Blind Controlled Trial);

Ex. 578, Tab 36 (Review - Post Transfusion Hepatitis - 66131369);

Ex. 578, Tab 37 (June 28, 1988, Recommendation of Blood Products Review Committee); and

Ex. 578, Tab 38 (Memo from Dr. Wark Boucher, Chief, Blood Products Division to Katherine Stewart, Project Officer, Research Administration Division, Extramural Research Programs Directorate dated June 30, 1988 re: Prevention of Non-A, Non-B Post-Transfusion Hepatitis by Screening Donor Blood for Anti-HBc and ALT: A Prospective, Radomized, Double-Blind Controlled Trial).

¹⁹⁹¹ Ex. 578, Tab 32, p. 3 (June 19, 1988, CRCS Proposal: Prevention of Non-A, Non-B Post-Transfusion Hepatitis by Screening Donor Blood for Anti-HBc and ALT: A Prospective, Radomized, Double-Blind Controlled Trial);

Ex. 578, Tab 33, para. IV. (June 21, 1988, CRCS Proposal: Prevention of Non-A, Non-B Post-Transfusion Hepatitis by Screening Donor Blood for Anti-Hbc and ALT: A Prospective, Radomized, Double-Blind Controlled Trial); and

1083. In addition, various U.S. transfusion experts appealed to Canada to pursue this vitally needed study. Supporters of the study included Drs. Alter (NIH)¹⁹⁹², Dr. Seeff (Georgetown University) and Dienstag (Harvard)¹⁹⁹³ and Dr. Katz (American Red Cross)⁹⁴²

6) Non-Scientific Factors: Political, Media, Legal Pressures

1084. The evidence of Drs. Blajchman and Perrault clearly indicated the view of the CRCS that the U.S. blood banking industry implemented NANB surrogate testing primarily for non-scientific reasons. The support the CRCS received from various U.S. transfusion experts only emphasized the fact that many within the American medical community recognized that the U.S. decision was motivated by political, media, legal and market pressures. U.S. blood bankers feared a backlash similar to that experienced during the early 1980's with AIDS. This included allegations that blood bankers were not doing enough to protect the safety of the blood supply. In addition, there was considerable market pressure on U.S. blood bankers to use surrogate testing as a promotional tool to gain an edge over their competitors. Pressure also came from test manufacturers who had an obvious vested interest in wide spread implementation of surrogate tests.⁹⁹⁵ As previously discussed, one of the many differences between the U.S.

Ex. 578, Tab 34, p.6 (June 20, 1988, CRCS Proposal: Prevention of Non-A, Non-B Post-Transfusion Hepatitis by Screening Donor Blood for Anti-Hbc and ALT: A Prospective, Radomized, Double-Blind Controlled Trial).

¹⁹⁹² *Ex. 579, Vol. 133, Tab 1 (February 17, 1987 letter from Dr. Alter, Chief, Immunology Section, Dept. of Transfusion Medicine Clinical Center to Dr. Perrault, former National Director BTS re: Surrogate testing issue).*

¹⁹⁹³ *Ex. 583, Vol. 136, Tab 20 (Seeff, L. and Dienstag J. et al., "Transfusion -associated non-A, non-B hepatitis: Where do we go from here?" Gastroenterology August 1988; 95(2):530-3).*

¹⁹⁹⁴ *Ex. 571, Vol. 132, Tab 66 (November 7, 1986 BTS Advisory Committee Minutes); and Evidence of Dr. Furesz, BoB Panel, pp. 43356-43357; 43366-43367; 43371; 43384-43385.*

¹⁹⁹⁵ *Evidence of Dr. Blajchman, Hamilton Centre Medical Director, p. 23022;*

Evidence of Dr. Perrault, former National Director BTS, pp. 29121-29122; 29172-29173; 29203; 30987-30996;

and Canadian blood systems was that the U.S. operated on a cost recovery basis enabling easier access to the financing necessary to implement surrogate testing.¹⁹⁹⁶

1085. Both Dr. Furesz¹⁹⁹⁷ of the BoB, and Dr. Irwin Walker¹⁹⁹⁸, former Chair of the Ontario CHS MSAC were convinced that the U.S. decision was based on non-scientific factors. In his NHRDP review of the Blajchman/Feinman study proposal, Dr. Zuck supported the CRCS principled decision to resist extraneous pressures. He wrote with approval, "This would be a major policy decision based on science rather than on other considerations."¹⁹⁹⁹ This was confirmed in his testimony when he acknowledged that non-scientific factors had a role to play in the U.S. decision to implement surrogate tests.²⁰⁰⁰

1086. Perhaps the most revealing evidence on this issue is the fact that in less than one month, the AABB, the CCBC, and the American Red Cross all reversed their initial decisions not to implement surrogate testing. In the absence of any new scientific evidence justifying such a move, a reversal on an issue of this importance in such a short period of time lends credence to the CRCS position that U.S. blood bankers endorsed surrogate testing as a matter of commercial necessity and not for its scientific validity. Others outside the CRCS also shared the opinion that the U.S. decision was made for the wrong reasons. This point is highlighted in a March 14, 1986 CCBC newsletter, where it is reported that the American Red Cross

Ex. 579, Vol. 133, Tab 28, p. 111 (Blajchman/Feinman study proposal: Research Project #88 - 760: Prevention of non-A, non-B post-transfusion hepatitis); and

Ex. 578, Tab 8 (April 2, 1986 memo from Dr. Alport, Medical Director, Regina Centre to Dr. Perrault, former National Director BTS re: NANB-Hepatitis, HTLV-III Notification, Chargeable Tests).

¹⁹⁹⁶ See discussion in Part A. Structure of Canadian Blood System - American System and B. Canadian Blood System Funding.

¹⁹⁹⁷ Evidence of Dr. Furesz, BoB Panel, pp. 43333; 43344; 43355-43356; 43365; 43384-43385.

¹⁹⁹⁸ Ex. 578, Tab 20 (May 1, 1987 CHS MSAC (Ontario Chapter) Annual Meeting Minutes).

¹⁹⁹⁹ Ex. 578, Tab 32 (June 19, 1988, CRCS Proposal: Prevention of Non-A, Non-B Post-Transfusion Hepatitis by Screening Donor Blood for Anti-HBc and ALT: A Prospective, Randomized, Double-Blind Controlled Trial).

²⁰⁰⁰ Evidence of Dr. Zuck, former Director of Division of Blood and Blood Products, FDA, p. 22572.

reversed its decision on surrogate testing after a meeting with its attorneys and communications staff.²⁰⁰¹

7) The Future of Surrogate Testing: Anti-HBc

1087. The Blajchman/Feinman study also concluded that there is no benefit to NANB surrogate testing in the post HCV testing era. They testified that it is now generally accepted that ALT testing is no longer a net contributor to the safety of the U.S. blood supply. They also noted that despite a body of recent U.S. opinion that anti-HBc testing may be of value in detecting rare post-transfusion HBV and some HIV window period cases, their study generated little data to support such theories.²⁰⁰²

8) Conclusion

1088. Documentary evidence and oral testimony given at the Commission reveal that the CRCS decision to pursue a study rather than implement NANB surrogate testing in the 1980's was not made in a vacuum. Various outside agencies and government bodies were consulted and endorsed the view that testing should only be implemented if Canadian data from a proper scientific study justified such a costly policy measure. Despite the political and legal pressure to simply follow the U.S. example on this issue, the CRCS course of action received significant support from the international blood transfusion community. The CRCS' decision, was reasonable and justified in light of the scientific controversy which existed at the time.

²⁰⁰¹ Ex. 722, pp. 2-3 (March 14, 1986 CCBC Newsletter).

²⁰⁰² Evidence of Dr. Blajchman, Hamilton Centre Medical Director, and Evidence of Dr. Feinman, Director, Hepatitis Research Laboratory, The Toronto Hospital, pp. 23271-23278.

